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CLINICAL INVESTIGATION SERVICE ANNUAL RESEARCH PROGRESS REPORT,--ETC(U)
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CLINICAL INVESTIGATION SERVICE

ANNUAL RESEARCH PROGRESS REPORT

FISCAL YEAR 1978

MADIGAN ARMY MEDICAL CENTER
TACOMA, WASHINGTON 98431

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ANNUAL PROGRESS REPORT

30 SEPTEMBER 1978

CLINICAL INVESTIGATION SERVICE

MADIGAN ARMY MEDICAL CENTER

TACOMA, WASHINGTON 98431

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TACOMA, WASHINGTON 98431

In conducting the research described in this report, the investigators adhered to the "Guide for Laboratory Animal Facilities and Care" as promulgated by the Committee on the Guide for Laboratory Animal Resources, National Academy of Sciences-National Research Council, and the "Guiding Principles in the Care and Use of Animals" approved by The Council of the American Physiological Society. The investigators followed the recommendations from the Declaration of Helsinki in the performance of investigations involving human subjects.

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CODE:

C - Completed
O - Ongoing
T - Terminated
P - Publication
PR - Presentation
SP - Submitted for publication

Work Unit Number: 78*/01**

* - Fiscal year in which registered
** - Chronological order of registration

FOREWORD

In order for the most modern medical care to be provided, a hospital and its staff need to have diligence and compassion in their work, basic skills, adequate equipment, continuing education, and knowledge of the recent progress in the medical arena. This knowledge can be partially acquired from reading the plethora of literature available. Often, however, this information is "old hat" by the time it reaches the mailbox. The most recent and applicable information comes from our own investigative contributions and the subsequent scientific exchanges that take place in the acquisition and presentation of this material. Also, dissemination of this information from Madigan to the rest of the medical community is more effective publicity for the military medical services than an advertisement in the "Yellow Pages." At Madigan we are fortunate to have this research facility available and to be able to provide the contribution to medical care which is important in fulfilling the mission of the hospital.

This report outlines some of the accomplishments in the field of clinical investigation during the past fiscal year. Research protocols described in this report were conducted under the provisions of AR 40-38, Clinical Investigation Program; AR 70-25, Use of Volunteers as Subjects of Research; and MAMC Supplement 1 to AR 40-38, Medical Services Clinical Investigation Program.

The staff at Clinical Investigation Service would like to express our appreciation for the support derived from the hospital during the past year in order to make these investigative procedures possible. I would like to thank Ms. Nancy Whitten for her efforts in compiling and preparing this report.

STEPHEN R. PLYMATE, M.D.
LTC, MC
Chief, Clinical Investigation Service

UNCLASSIFIED

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18. SUPPLEMENTARY NOTES

The findings in this report are not to be construed as an official Department of the Army position unless so designated by other authorized documents.

19. KEY WORDS (Continue on reverse side if necessary and identify by block number)

Unit summary; research protocols (objective, method, progress, status); publications; presentations; U.S. Army Preceptorship Program in Comparative Medicine

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

Subject report identifies those individuals who are conducting investigative protocols at Madigan Army Medical Center. An abstract of each protocol giving abbreviated technical objectives, methods, and progress is presented.

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CLINICAL INVESTIGATION SERVICE

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PUBLICATIONS FY 78

CLINICAL INVESTIGATION SERVICE

Crumrine, M.H., Balk, M.W., and Fischer, G.W.: Immunologic Cross Reactivity Between Type III Group B Streptococci and Type 14 Streptococcus pneumoniae (Abstract). Abstracts of the Annual Meeting of the American Society for Microbiology, 14-19 May 78, p 61, #E111.

Heggers, J.P., Hinrichs, D.J., Mallavia, L.P., and Robson, M.C.: Pathophysiologic Features of Q Fever-Infected Guinea Pigs (Abstract). Abstracts of the Annual Meeting of the American Society for Microbiology. 14-19 May 78, p 16, #B-15.

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DENTAL ACTIVITY

Jones, G.B.: The Use of Silastic as an Injectable Root Canal Obturating Material. Submitted to J Endodontics, Jan 78.

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PHYSICAL MEDICINE AND REHABILITATION SERVICE

Budurowich, M. and Lofton, W.: Occupational Therapy Program for Diabetics. Submitted to Diabetes Care, Aug 78.

DEPARTMENT OF PSYCHIATRY

Parker, R.A.: The Fort Lewis Smoking Control Clinic: A Major Follow-Up Study. Submitted to Prof Psychology, Jun 78.

PRESENTATIONS FY 78

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Heggers, J.P. and Krieg, R.E.: The Effect of Mycobacterium ulcerans Toxin on Mammary Gland Adenocarcinoma Implants in C3H/HeJ Mice. Annual Meeting of the Association of Military Surgeons of the United States, 27 Nov-1 Dec 1977, Washington, DC.

Heggers, J.P., Billups, L.H., Hinrichs, D.J., and Mallavia, L.P.: Pathophysiologic Features of Q Fever-Infected Guinea Pigs. Annual Meeting of the American Society for Microbiology, 15-19 May 1978, Las Vegas, NV.

Heggers, J.P., Jennings, P.B., Krieg, R.E., and Robson, M.C.: The Effect of Mycobacterium ulcerans Toxin on Mammary Gland Adenocarcinoma Implants in C3H/HeJ Mice. Annual Meeting of the American Society for Microbiology, 15-19 May 1978, Las Vegas, NV.

Heggers, J.P., Jennings, P.B., Krieg, R.E., and Robson, M.C.: The Effect of Mycobacterium ulcerans Toxin on Mammary Gland Adenocarcinoma Implants in C3H/HeJ Mice. American Veterinary Medical Association Meeting, 16-20 July 1978, Dallas, TX.

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Jennings, P.B.: Physical Examination, Presurgical Sample Taking, and Evaluation of Clinical Lab Samples in the Surgical Patient. Fifth Annual Veterinary Surgical Forum, 26-28 Oct 1977, Chicago, IL.

Jennings, P.B.: Rationale for the Use of Antibiotics in the Shock Patient. Fifth Annual Veterinary Surgical Forum, 26-28 Oct 1977, Chicago, IL.

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Jennings, P.B., Knudson, R.P., Alden, E.R., and Crumrine, M.H.: Evolution and Evaluation of a Heel-Stick Blood Culture Technique for Neonatal Use (Exhibit). American Academy of Pediatrics - Spring Session, April 1978, Los Angeles, CA.

Jennings, P.B., Alden, E.R., and Henderson, R.W.: Intubate a Kitten - Resuscitate a Baby (Exhibit). Third Annual Conference on Neonatal and Perinatal Medicine, 18-20 May 1978, Reno, NV.

Jennings, P.B., Knudson, R.P., Alden, E.R., and Crumrine, M.H.: Evolution and Evaluation of a Heel-Stick Blood Culture Technique for Neonatal Use (Exhibit). American Medical Association Meeting, 12-16 June 1978, St Louis, MO. Won Certificate of Merit.

Jennings, P.B., Knudson, R.P., Alden, E.R., and Crumrine, M.H.: Blood Culture Techniques - Micromethods. American Medical Technologists Meeting, 13 Jul 1978, Chicago, IL.

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Ridgway, R.L. and Zielke, D.R.: Instrumentation, Nonsurgical Repair and Preservation of Fractured Anterior Teeth in Dogs - Canine Endodontics (Autotutorial Program). American Veterinary Medical Association Meeting, 16-20 July 1978, Dallas, TX.

Roth, R.R. and Usry, R.T.: Cryopreservation of Human Platelets: A Modified Glycerol-Glucose Method. Third Annual Meeting of the Society of Armed Forces Medical Laboratory Scientists, 4-6 October 1977, Williamsburg, VA.

Roth, R.R. and Usry, R.T.: Cryopreservation of Human Platelets: A Modified Glycerol-Glucose Method. Advanced Component Seminar of the Haemonetics Research Institute, 19-21 June 1978, Boston, MA.

Thomas, S.R., Heggers, J.P., Morrison, R., and Garrison, M.: Evaluation of the Antiseptic, Sanitary and Practical Utilization of Septisol, Alcare, and Triclean Under Simulated Combat Conditions. (Exhibit.) Association of Military Surgeons of the United States Meeting, 27 Nov-1 Dec 1977, Washington, DC.

Ward, G.S.: Asepsis and Surgical Procedures. (Lecture) Department of Pathology and Microbiology, Division of Animal Medicine, School of Medicine, University of Washington, 17 Feb 1978, Seattle, WA.

DENTAL ACTIVITY

Stanley, P.: Relationship of the Pulp Chamber to the External Surface of the Furcation of Mandibular First and Second Molars. Univ of Washington Center for Research in Oral Biology Annual Research Conference, 12 June 1978, Seattle, WA.

DEPARTMENT OF FAMILY PRACTICE

Auer, T.H., Holtzapple, K., Hollison, R.B., and Stuart, R.: The Doctor-Patient Relationship: Critical Elements. Univ of Washington Family Practice Residency Network Meeting, April 1978, Seattle, WA.

Auer, T.H., Holtzapple, K., Hollison, R.B., and Stuart, R.: The Doctor-Patient Relationship: Critical Elements. Uniformed Services Chapter of the American Academy of Family Practice Annual Meeting, April 1978, Jacksonville, FL.

DEPARTMENT OF PEDIATRICS

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Espinoza, J.L., Tuttle, W.K., Toews, W.H., and Atkinson, A.W.: Quantitation of Left to Right Shunts Using the Gamma Variate Function in a Typical Nuclear Medicine Clinic. Annual Spring Meeting of the Pacific Northwest Chapter of the Society of Nuclear Medicine, 15 April 1978.

Ortiz, Amil: Oxygen Consumption Under Overhead Warmers and in Isolettes. Third Annual Conference on Neonatal-Perinatal Medicine, 18-20 May 1978, Reno, NV.

DEPARTMENT OF PATHOLOGY

Back, A.E. and Oberhofer, T.R.: Biotypes of Haemophilus Encountered in the Clinical Microbiology Laboratory. 78th Annual Meeting of the American Society for Microbiology, 14-19 May 1978, Las Vegas, NV.

Oberhofer, T.R.: Comparison of the API 20-E and Oxiferm Systems with a Conventional Method in the Identification of Nonfermentative Bacteria. 78th Annual Meeting of the American Society for Microbiology, 14-19 May, Las Vegas, NV.

UNIT SUMMARY FY 78

1. Objective

To provide the facilities and environment to stimulate an interest in clinical and basic investigations within Madigan Army Medical Center.

2. Technical Approach

MANPOWER

DESCRIPTION	RANK	MOS
Chief Plymate, Stephen R., MC	05	61C9B
Vet Lab Officer Ward, George S., VC	04	64C00
Bacteriologist Crumrine, Martin H., MSC	03	68A9C
Physiologist Jacob, Willis H., MSC	03	68J9C
Biochemist Smith, Michael L., MSC	03	68C9C
NCOIC Lindstrom, Duane E.	E7	92B40
Med Lab Spec Naegle, Debbra	E5	92B30
Vet Anim Spec Lee, Donald R.	E4	91T20
Vet Anim Spec Pack, Donald L.	E4	91T20
Vet Anim Sp Clark, Gerald	E3	91T20

DESCRIPTION	RANK	MOS
Med Tech, Supervisor Graves, James N.	GS9	00644
Med Tech Garrison, Mina J.	GS7	00644
Med Tech Matej, Louis A.	GS7	00644
Edit Asst/Steno Whitten, Nancy J.	GS6	00318
Clerk Steno Fraser, Elizabeth L.	GS4	00312
Animal Caretaker Mallouf, Jerry L.	WG6	07706

	FUNDING
MEDCASE Equipment	$64,811.00
Capital Equipment	938.00
Personnel Services (Civilian salaries)	85,681.00
Consumable Supplies	28,960.10
Temporary Duty Travel	1,925.13
Contractual Services	4,435.90
TOTAL	$186,751.13

3. Progress

During FY 78 there were 144 active protocols. Of these, 107 are presently ongoing; 11 completed; and 26 terminated.

There were 35 publications and 27 presentations (including exhibits and autotutorials) at national meetings reporting work performed at Madigan Army Medical Center under the sponsorship of the Clinical Investigation Service. Eight manuscripts have been submitted for publication on which no decision has been received from the journal.

U.S. Army Preceptorship Program in Comparative Medicine for U.S. Army Veterinary Corps Officers

MAJ George S. Ward, VC
Clinical Investigation Service
Director

On 15 August 1973 the United States Army Preceptorship Program in Comparative Medicine for United States Army Veterinary Corps officers was approved by the Surgeon General's Senior Review Committee, and begun at Madigan Army Medical Center. The purposes of the program are:

1. To provide and train Veterinary Corps officers to staff the Clinical Investigation facilities.

2. To provide clinical scientists and teachers to assist in the training of physicians, dentists, and other biological scientists in research procedures and the selection and use of animal models for human disease problems.

3. To provide training for Veterinary Corps officers in laboratory animal medicine as it applies to Clinical Investigation facilities. To insure that the facilities and the health and treatment of laboratory animals in Army facilities are in accordance with American Association for Laboratory Animal Science standards.

4. To provide opportunity for clinically-oriented Veterinary Corps officers to acquire further training in veterinary medicine and surgery, especially as it applies to human public health.

5. To provide a group of experienced teachers for training nursing and medical enlisted personnel in emergency first aid procedures in a laboratory environment.

6. To increase the quality and quantity of military medicine-oriented protocols emanating from Clinical Investigation facilities.

7. To foster military-civic affairs in the communities surrounding military medical facilities.

There have been three graduates of the CMP Program. Due to a shortage of personnel in the Veterinary Corps, a preceptee has not been assigned to this program since July 1977.

DETAIL SHEETS
FOR
PROTOCOLS

TITLE: A Teaching Model for Pediatric Intubation Utilizing Ketamine-Sedated Kittens

PRINCIPAL INVESTIGATOR: LTC Errol E. Alden, MC

WORK UNIT NO: 74/19

TECHNICAL OBJECTIVE

To teach infant resuscitation procedures to nurses, nurse clinicians, OB GYN residents, and other nonpediatric physicians who may be called upon to treat pediatric emergencies. Many physicians and paramedics have never had the training opportunity to attempt intubation of an awake living creature. The kitten, immobilized with ketamine hydrochloride, gives the student the opportunity to visualize vocal cords, precipitate laryngospasm, and learn the difficulties associated with emergency intubation.

METHOD

Weaned kittens, weighing 0.5 to 1.0 kg will be used in these teaching sessions. Ketamine hydrochloride (22 mg/kg) plus atropine sulfate (0.04 mg/kg) will be administered intramuscularly to each kitten. Intubation will be performed with the kittens on their backs, using a pediatric laryngoscope, and sizes 8 through 14 French endotracheal tubes. Kittens may be used for several consecutive weekly sessions until they grow too large to be utilized. The procedure is not harmful to the kittens.

PROGRESS

(77 10 - 78 09) Due to the departure of LTC Paul B. Jennings, VC, the project has been taken over by LTC Errol E. Alden, MC, Department of Pediatrics, MAMC. Regular teaching sessions are still being conducted for MAMC personnel.

The teaching model was incorporated into a scientific exhibit, entitled "Teaching Models for Neonatal Resuscitation" which has received several awards at national meetings in prior years and was displayed at the Annual Meeting of the Association of Military Surgeons of the United States in Washington, 27 Nov - 1 Dec 77 and at the Third Annual Conference on Neonatal and Perinatal Medicine in Reno, Nevada, 18-20 May 78.

STATUS: (O)

TITLE: Characterization of the Antigenic Similarities of Group B Streptococci and Streptococcus pneumoniae

PRINCIPAL INVESTIGATOR: CPT Martin H. Crumrine, MSC

WORK UNIT NO: 78/48

TECHNICAL OBJECTIVE

To further deliniate the antigenic similarities between type III Group B streptococci and Streptococcus pneumoniae.

METHOD

1. To isolate and purify GBS antigens and Pn. antigens.
   a. Organisms will be cultured in a chemically defined medium.
   b. Antigens will be extracted, using several techniques, and fractionated.
   c. Protein DNA and RNA will be removed from the carbohydrate antigens.
   d. The antigen then will be concentrated by lyophilization.
2. The following antibodies will be produced in rabbits.
   a. Whole cell GBS and Pn. antibody.
   b. Antibodies against each of the type specific whole cell antigens of the 5 types of GBS and several pneumococcal types.
   c. Antibodies against various type specific polysaccharides.
3. Comparisons of all 5 GBS types with various Pn. antisera and Pn. antigens with GBS type specific antisera and GBS whole cell antisera using the following techniques: immunodiffusion, immunoelectrophoresis, agglutination, quellung reaction, chemiluminescence, opsonophagocytic activity, and animal protection tests.
4. To characterize the cross reactive antigenic sites using specific mono- and oligosaccharides to demonstrate the similarities of the antigenic sites.
5. To determine if any cross reactive antigens are in the pneumococcal vaccine using the techniques described above.

Characterization of the Antigenic Similarities of Group B Streptococci and Streptococcus pneumoniae - Crumrine

PROGRESS

(78 08 - 78 09) This project has not been activated due to the lack of funds for expendable supplies. Anticipate that this project will begin in FY 79 when funds become available.

STATUS: (O)

TITLE: Renal Glycosuria: Evaluation of Renal Function, Carbohydrate Metabolism and Possible Development of Diabetes Mellitus

PRINCIPAL INVESTIGATOR: COL Bruce L. Fariss, MC

WORK UNIT NO: 69/01

TECHNICAL OBJECTIVE

To study patients with renal glycosuria in an attempt to further classify these patients. More importantly, we shall attempt to distinguish those patients who may develop diabetes mellitus by studying responses to oral glucose and intravenous glucose and tolbutamide with measurement of blood and urine glucose and insulin levels. The patients will be reevaluated at yearly intervals up to five years to determine the incidence of diabetes mellitus.

METHOD

Forty patients who are found to have flat or normal oral glucose tolerance tests with renal glycosuria shall be evaluated.

Day 1: History, physical examination, routine CBC, chest x-ray, STS, regular hospital diet (300 gm CHO).

Day 2: Twenty-four hour urine for Na, K, CO_2, Cl_2, Ca, P, SGOT, alkaline phosphatase, BUN, creatinine, uric acid and serum electrophoresis. Urinary pH measured at each voiding.

Day 3: Oral glucose tolerance blood and urine glucose and plasma insulin levels.

Day 4: Intravenous glucose tolerance test (25 gm), blood and urine glucose and plasma insulin.

Day 5: Infusion of glucose, intravenous to calculate the splay (renal tubular reabsorption as a function of lead presented to the tubule). Inulin and endogenous creatinine clearances to be done in conjunction with the glucose infusion.

Day 6: Day of rest.

Renal Glycosuria - Fariss

Day 7: Tolbutamide tolerance test (1.0 gm I.V.) specimens for glucose and insulin at 0, 2, 15, 30, 45, 60, 90, 120, 150, and 180 minutes.

Day 8, 9, and 10: NH_4Cl loading p.o. with measurement of hydrogen secretory capacity, net acidification and ammonia production each day.

PROGRESS

(77 10 - 78 09) This study includes 49 individuals with renal glycosuria and continues to be ongoing with subjects being contacted yearly. Two individuals have developed diabetes mellitus.

STATUS: (O)

TITLE: The Effects of Chronic Hyperglycemia on Pregnancies and Fetuses in Sheep During Gestation

PRINCIPAL INVESTIGATOR: COL Bruce L. Fariss, MC

WORK UNIT NO: 74/08

TECHNICAL OBJECTIVE

The objectives of this project are to determine the effect of hyperglycemia upon pregnancies as manifested by frequency of abortions and hydramnios and possible developmental abnormalities of the fetuses.

METHOD

The study will be composed of three groups of pregnant ewes with as close proximity of the date of conception as possible. All groups will be given food and water ad lib.

1. The control group will be comprised of six animals with no treatment.

2. Group #2 will be composed of seven animals which have undergone subtotal pancreatectomy. The diabetes mellitus produced surgically will be managed by the injection of intermediate acting insulin such as NPH. Blood sugars will be monitored frequently as indicated clinically.

3. The third group will be composed of seven animals which have indwelling catheters for infusion of hypertonic sugar solutions with a lambda infusion system. The systems are portable, weighing less than 3 lbs and can be strapped to the backs of the animals without difficulty. Blood sugars will be monitored at frequent intervals with an attempt to keep blood sugars between 200 and 300 mg/100 ml of blood at all times.

The course of the pregnancies will be observed for each group of animals. Blood sugars for each group will be determined at frequent intervals during the gestation. At delivery the neonate will be examined pathologically for evidence of pulmonary, liver, pancreatic, kidney, and possible developmental abnormalities.

The Effects of Chronic Hyperglycemia - Fariss

PROGRESS

(77 10 - 78 09) Approximately 99% of the pancreas was resected in thirteen sheep. Intravenous glucose tolerance tests were abnormal. All fetuses died within two weeks after delivery. No histological or pathological abnormalities were found.

It was observed that total pancreatectomy in twelve sheep was not associated with hyperglycemia; however, intravenous glucose tolerance tests were abnormal. Alloxan does produce hyperglycemia.

It was found that serum zinc levels were elevated in sheep following total pancreatectomy or pancreatic duct ligation in contrast to alloxan treated sheep and controls.

A paper has been written entitled, "The Effect of Total Pancreatectomy, Pancreatic Duct Ligation, and the Administration of Alloxan on Serum Zinc Levels in Sheep," to be submitted to The Proceedings of Experimental Biology and Medicine.

STATUS: (O)

TITLE: Evaluation of the Cyclic Nature of Human Semen Content

PRINCIPAL INVESTIGATOR: CPT Willis H. Jacob, MSC

WORK UNIT NO: 78/34

TECHNICAL OBJECTIVE

To determime semen quality by measuring sperm count, sperm motility, sperm morphology, and various constituents of seminal fluid. These findings will then be analyzed for cyclic patterns.

METHOD

1. Test Subjects: Twenty to thirty healthy volunteers will be selected from the 9th Infantry Division or the 62nd Medical Group. Selection will be based on physical examination and medical history. Individuals will be excluded from the project for any of the following reasons: evidence of active venereal disease; a history of testicular varicocele; currently using the sauna on a regular basis; currently taking any medication; any adverse finding during the physical examination. Volunteers will abstain from the use of alcohol and other drugs throughout the semen collection phase of the project. Volunteers will abstain from sexual intercourse for a period beginning 48 hours before collection of the first semen sample and extending throughout the sample collection period.

2. Semen Collection and Analysis: Semen samples will be collected daily for a period of 20 to 25 days. Samples will be collected during a specified 30-minute period each day. The semen, obtained through masturbation, will be ejaculated directly into plastic containers which are free of trace metals. The samples will be allowed to liquefy for one hour at room temperature (24°C). The liquefied samples will be measured for volume and color, and then will be divided into two portions. One portion will be assayed immediately for viscosity, sperm count, sperm motility, and sperm morphology. The other portion of the samples will be centrifuged and the sperm-free seminal fluid will be retained for assay of seminal fluid constituents to include prostaglandins, gonadotropins, trace metals, and carbohydrates.

Evaluation of the Cyclic Nature of Human Semen Content - Jacob

PROGRESS

(78 07 - 78 09) Equipment and supplies are now being procured for this project. When all technical procedures are operational, volunteers will be recruited and the project will begin.

STATUS: (O)

TITLE: Correlation of the Effects of Semen Sperm Count and Prostaglandin Content on Fertility in Human Males

PRINCIPAL INVESTIGATOR: CPT Willis H. Jacob, MSC

WORK UNIT NO: 78/45

TECHNICAL OBJECTIVE

The objective of this study is to compare the semen quality of men of known fertility to that of men who are apparently infertile. The parameters of semen quality will be sperm count, sperm motility, sperm morphology, sperm viability, seminal prostaglandins, seminal fructose, seminal zinc, seminal gonadotropins, and gonadal steroids. Seminal prostaglandin content will be compared with each of these parameters.

METHOD

Semen specimens will be collected from 20-25 volunteers of known fertility and from 20-25 volunteers with apparent infertility. Following a urological evaluation, each volunteer will be asked to provide three semen specimens. Each volunteer will provide a semen specimen following a 48-hour period of abstinence from sexual activity. Subsequent samples, obtained at the end of a 48-hour abstinence period, will be given at one-week intervals for a two-week period. Each volunteer will ejaculate directly into a plastic container which is free of trace metals. The specimens will be analyzed for volume, color, sperm count, sperm motility, sperm morphology, prostaglandins E, prostaglandins F, and various other seminal fluid constituents. The prostaglandin content will be compared with the sperm analysis for correlation. Prostaglandin content will also be compared to other seminal fluid components such as fructose, zinc, gonadotropins, and gonadal steroids.

PROGRESS

(78 08 - 78 09) Equipment and supplies are now being procured for this project and volunteers are being recruited. Technical procedures are being made operational.

STATUS: (O)

TITLE: Clinical Trials of a Peripheral Capillary Blood Culture Sampling Technique

PRINCIPAL INVESTIGATOR: MAJ Richard P. Knudson, MC

WORK UNIT NO: 76/28

TECHNICAL OBJECTIVE

To compare the effectiveness of a new peripheral capillary blood culture sampling technique with standard blood culture methods in human neonatal and adult patients. This technique has been demonstrated effective in three animal species and needs clinical trials to determine whether it may be used as a supplemental sampling method in man.

METHOD

GROUP I - Neonatal Patients

Infants suspected of having transient bacteremia or frank sepsis will be sampled for blood culture in the usual manner. In addition, peripheral capillary blood will be sampled at the same time via heel stick, and the results will be compared to those achieved by the standard method. Blood for pour plates will also be drawn.

GROUP 2 - Adult Patients

The capillary blood culture technique (finger stick) consists of meticulous skin preparation and drawing of 0.1 - 0.2 ml of blood into a heparinized tuberculin syringe with 20 gauge needle attached. The needle is changed and the blood is injected into a standard blood culture bottle. Results are read at 24 and 48 hours and subcultures are performed where necessary.

Routine blood culture will also be performed in each case.

A population of adult patients undergoing urological instrumentation in the Urology Service will be sampled before their procedure and at 5, 15, and 30 minutes following the procedure,

Clinical Trials of a Peripheral Capillary Blood Culture Sampling Technique - Knudson

comparing standard blood culture technique and the capillary blood culture sampling technique. Patients undergoing trans-urethral resection of the prostate, urethral dilation, prostatic biopsy, cystoscopy, and other urological manipulations are felt to have a relatively high incidence of bacteremia.

PROGRESS

(77 10 - 78 09) MAJ Richard P. Knudson, MC, has been appointed as principal investigator on this protocol due to the departure of LTC Paul B. Jennings, VC.

Clinical trials of the method are continuing. Correlation of the heel-stick blood culture technique (with standard sampling using larger volume of blood) has been good and contamination has not been a problem. Approximately 75% of the patients have been tested and the testing should continue for approximately one more month.

A scientific exhibit entitled "Evolution and Evaluation of a Heel-Stick Blood Culture Technique for Neonatal Use" has been constructed as a result of this protocol. This exhibit has been displayed at several national meetings, including the Meeting of the American Medical Association, St. Louis, Missouri, 17-21 Jun 78, where it was awarded a Certificate of Merit.

STATUS: (O)

TITLE: Glucose Homeostasis in Pregnancy and its Relationship to Gestation and Infant Well Being

PRINCIPAL INVESTIGATOR: MAJ Wijdan A. Luqman, MC

WORK UNIT NO: 78/37

TECHNICAL OBJECTIVE

The diagnosis of diabetes has had different criteria during pregnancy. The objective of this study is to identify and analyze the risk factors and mechanisms associated with hyperglycemia and other problems of glucose metabolism during pregnancy.

METHOD

Retrospective studies will be undertaken. These will be done on clinical data obtained from patients' records, e.g., correlations between blood glucose values, birth weight, outcome of pregnancy, etc. The records utilized will be past records (2 years) available at Madigan Army Medical Center. Patients' involvement will not be required nor will patients be required to undergo any tests. Records will be reviewed by physicians involved and data analyses will be examined by statistical methods. Non-physician assistants will be involved in data analyses only. Identification of risk factors and mechanisms of disease will be analyzed by computer and statistical analysis.

PROGRESS

(78 05 - 78 09) This study is on-going and the results are being analyzed. An additional assistant is being incorporated and statistical assistance is being sought.

Two papers have been submitted for consideration for publication from the results obtained to date. A presentation entitled "A Fetal Weight Determinant Based on Maternal Glycemia and Positive Caloric Balance in Non-diabetic Women" will be presented at the 17th Annual Meeting of the Armed Forces District of the American College of Obstetrics and Gynecology and the 27th Armed Forces Seminar on Obstetrics and Gynecology (combined meeting), Fall 78, Washington, DC.

STATUS: (O)

TITLE: Adrenocortical Reserve in Patients with Metastatic Carcinoma

PRINCIPAL INVESTIGATOR: MAJ K. David McCowen, MC

WORK UNIT NO: 76/05

TECHNICAL OBJECTIVE

To evaluate the adrenocortical reserve in patients with metastatic carcinoma by alpha 1-24 ACTH stimulation.

METHOD

Patients with documented metastatic carcinoma (lungs, bone, etc.) will be tested with alpha 1-24 ACTH (Cortrosyn^{R}) according to common clinical procedures after baseline serum cortisol levels have been obtained. In those patients demonstrating a suboptimal adrenal reserve, repeat stimulation will be performed after chemotherapy has been given to detect improvement in the reserve function of the adrenal gland.

PROGRESS

(77 10 - 78 09) Non-treated patients with metastatic carcinoma continue to be examined for depressed adrenocortical reserve. No adrenal insufficiency has been determined to date.

STATUS: (O)

TITLE: The Role of Thyroid Suppression in the Treatment of Thyroid Cysts

PRINCIPAL INVESTIGATOR: MAJ K. David McCowen, MC

WORK UNIT NO: 76/18

TECHNICAL OBJECTIVE

To evaluate the efficacy of thyroid suppression in the treatment of benign thyroid cysts.

METHOD

All patients with suspected thyroid nodules will be referred to the Thyroid Clinic where evaluation of the nodule with palpation, radionuclide scanning, and ultrasonography will be performed. Blood studies to include T_3RAIU, T_4CPB, Serum T_3, and thyroid antibodies will be done. Those patients with cystic lesions as shown by these studies will undergo percutaneous needle aspiration of these cysts. Aspiration of thyroid cysts is performed routinely in our clinic. The aspirated fluid will be evaluated with cytological examination.

The patients with successful aspirations will be entered into the experimental protocol as follows. Patients in sequence will be referred to a disinterested party who will have a series of sequenced random numbers. If the patient's random number is even, he will be started on an equivalent of three grains of desiccated thyroid hormone, and, if his random number is odd, he will be started on an identical placebo. The patients will be followed for a minimum of one year. A minimum of 20 patients will be utilized for the study. All patients not entered into the study will undergo appropriate therapy in the conventional manner.

PROGRESS

(77 10 - 78 09) Twenty patients with thyroid cysts are now being followed for recurrence after aspiration. They have been assigned to either thyroid suppression or placebo medication to determine the efficacy of therapy in the prevention of thyroid cyst recurrence.

STATUS: (O)

TITLE: Testicular Dihydrotestosterone (DHT) and Testosterone (T) Levels in Oligospermic Patients with Varicoceles

PRINCIPAL INVESTIGATOR: MAJ K. David McCowen, MC

WORK UNIT NO: 77/02

TECHNICAL OBJECTIVE

To determine if a difference in the testicular tissue level of T and DHT exists between the affected and normal testes of oligospermic varicocele patients.

METHOD

Patients requiring high ligation of the spermatic vein will be identified. Preparatory studies will include a semen analysis, serum testosterone, FSH and LH levels. After counseling the patient and after being granted informed consent, biopsy of both the affected and normal testes will be done at the time of the indicated surgery for varicocele repair. The tissue (50-100 mg per biopsy) will be received by the principal investigator or his designee for analysis. The tissue will be examined by extraction, separation, and radioimmunoassay of the T and DHT. A total of 20-25 patients will be studied and the comparison of these steroids from each of the patient's testes will be made, with the patient serving as his own control.

PROGRESS

(77 10 - 78 09) The project has successfully established testicular tissue testosterone and dihydrotestosterone levels in subfertile males with varicocele. This work has been published in abstract form and has been accepted for publication in Fertility - Sterility.

STATUS: (C)

TITLE: The Effect of Aspirin on Blood and Urine Thyroxine in Induced Canine Hyperthyroidism

PRINCIPAL INVESTIGATOR: MAJ K. David McCowen, MC

WORK UNIT NO: 77/03

TECHNICAL OBJECTIVE

To evaluate the effect of aspirin on the fate of serum and urine thyroxine in mongrel dogs with induced hyperthyroidism.

METHOD

Ten mongrel dogs will be utilized. The dogs will be paired and given 1.0 mg LT_4 intravenously 24 hours before receiving 1.2 mg ASA, orally, on the morning of the study. One dog will receive the ASA with the other receiving only LT_4. Baseline serum T_4 levels will be drawn and repeated at 30 minute intervals, 2 hours to 4½ hours after the ASA is given. Urine T_4 levels will be determined at 30 minute intervals, 2 hours to 4½ hours after the ASA is given, and serum ASA levels will be determined at 3 hours after administration. Six weeks later, the same pair of dogs will be studied in identical fashion, with the exception that control dogs will receive the ASA with the other dog serving as the control. T_4 levels will be determined by RIA in the Clinical Investigation Laboratory.

PROGRESS

(77 10 - 78 09) This project is presently undergoing technical modification as the original procedures and animal models involved are not applicable to existing technology.

STATUS: (O)

TITLE: The Effect of Exogenous Glucocorticoids on FSH-LH Levels in Post-Menopausal Females

PRINCIPAL INVESTIGATOR: MAJ K. David McCowen, MC

WORK UNIT NO: 77/04

TECHNICAL OBJECTIVE

To determine if oral glucocorticoids suppress gonadotropin excretion by their action on the hypothalamic-pituitary axis.

METHOD

Post-menopausal patients with intact ovaries who are not ingesting exogenous estrogens will be studied. These patients will be selected in the Rheumatology Clinic from those patients requiring treatment with oral glucocorticoids for non-endocrine related disease, such as rheumatoid arthritis, SLE, and polymyalgia rheumatica. After obtaining informed consent, blood will be drawn before, during, and after glucocorticoid therapy for FSH-LH determinations. The effect of these exogenous glucocorticoids on the high endogenous post-menopausal FSH-LH levels will then be determined.

PROGRESS

(77 10 - 78 09) This project has been terminated due to a lack of clinical material.

STATUS: (T)

TITLE: Comparison of the Protein-Sparing Modified Fast with Conventional Dietary Therapy in the Treatment of Obesity

PRINCIPAL INVESTIGATOR: MAJ K. David McCowen, MC

WORK UNIT NO: 78/07

TECHNICAL OBJECTIVE

This protocol will explore the efficacy of treating obese patients with an outpatient experimental diet as compared with conventional diet therapy as currently administered by Diet Therapy at MAMC. This study will address the initial rate of weight loss, the success of chronic therapy in maintaining the achieved lower weight, the problem of loss of muscle (protein) mass resulting in fatigue and poor compliance, and the psychological variables in individuals being treated for obesity to seek ways of psychological intervention which might increase the effectiveness of the diet regime.

METHOD

Adult obese patients 30% above ideal body weight (IBW) will be identified and referred for evaluation. A complete physical examination and a biochemical screen will then be done. Patients will be randomly assigned to either the Protein-Sparing Modified Fast (PSMF) (1.5 gm/kg/IBW/day lean protein plus prenatal vitamins one/day; Titralac tablets 2 bid; K-lyte one/day) or a conventional 1000 calorie diet. The patients will be seen by the contact physician every month for a follow-up SMAC-20 and reassessment. Five standard psychological assessment procedures will be given before the beginning of diet therapy, after weight reduction to approximately 50% of IBW, when IBW is reached, approximately three months after reaching IBW. Upon achievement of IBW, the patients will be entered on maintenance programs and followed for a period of 9 months.

PROGRESS

(77 12 - 78 09) The technical portion of this project has been completed, and the data are now being examined. The initial observations include a lack of morbidity in either dietary group, more rapid weight loss in the PSMF group, and a greater overall success rate in the conventional dietary group.

STATUS: (O)

TITLE: Association of Hypercalcemia, Hypertension, and the Use of Thiazide Diuretics

PRINCIPAL INVESTIGATOR: MAJ Edward J. Przasnyski, MC

WORK UNIT NO: 78/33

TECHNICAL OBJECTIVE

To perform a retrospective analysis of a group of hypertensive patients in order to discover the incidence of hypercalcemia, whether it is reversible, and if it is associated with the use of thiazide diuretics.

METHOD

A large group of hypertensive patients seen by the nurse clinician in the hypertensive clinic over the past eight months (approximately 1500) will have their charts reviewed to determine the incidence of hypercalcemia, association of the hypercalcemia with medications (notably thiazide diuretics), and to arrange follow-up to determine the etiology of the hypercalcemia.

Patients with hypercalcemia on two occasions within the past one year will be evaluated in the Endocrine Clinic if the hypercalcemia persists after discontinuing thiazides for one month.

PROGRESS

(78 04 - 78 09) Approximately 350 patients have been screened for hypercalcemia. Between 15-20% have slight to moderate increased calciums and one-third have repeat elevated calciums after thiazides have been discontinued (6 weeks). To date, 26 patients are being evaluated with persistent hypercalcemia. The future plan is to review and screen another 500-700 patients. Completion is anticipated within the next 6-9 months.

STATUS: (O)

TITLE: Gonadotropin Responses to Gonadotrophic Releasing Hormone as Predictor of Fertility in Oligospermic Males Treated with Clomiphene Citrate

PRINCIPAL INVESTIGATOR: MAJ Edward J. Przasnyski, MC

WORK UNIT NO: 78/50

TECHNICAL OBJECTIVE

To determine whether gonadotropin responses in men with oligospermia before or during treatment with clomiphene citrate will predict those who will eventually respond with increased fertility.

METHOD

Fifteen to twenty-five males who meet the following criteria will be entered into the protocol: (1) three sperm counts $<15 \times 10^6$ with three days abstinence prior to sample collection; (2) good general health, on no medications and evidence of normal sexual function present; (3) wives have been carefully evaluated and are normal or fertility problems corrected; (4) normal serum testosterone, prolactin, and LH levels; and (5) normal FSH level.

Normal FSH level will be determined from three pooled samples collected at 30 minute intervals. Three FSH, LH levels will be drawn at 15 minute intervals and then patients will be given a baseline GNRH bolus. FSH, LH will then be drawn at 15, 30, 45, 60, 90, 120, and 180 minutes after the bolus. The patients will then be started on clomiphene citrate 25 mg daily for 25/30 days for a minimum of six months. GNRH testing will be completed as described above during the second and fourth months of therapy. The patients will have monthly sperm analyses, and serum testosterone, LH and FSH levels will be drawn monthly. Patients will be continued on clomiphene citrate up to 12 months if a response (increased counts by 25-50%) is demonstrated in the first six months. A patient will be dropped from the study group at six months if no respomse to clomiphene is seen or if the wife becomes pregnant.

PROGRESS

This project is awaiting approval from the Human Use Review Office and therefore no work has been done on it.

STATUS: (O)

TITLE: Cryopreservation of Human Platelets for Transfusion

PRINCIPAL INVESTIGATOR: MAJ Rob R. Roth, MC

WORK UNIT NO: 77/06

TECHNICAL OBJECTIVE

To preserve platelets for transfusion by freezing.

METHOD

Phase I. Freeze and recover platelets.

a. Screen 10 healthy routine blood donors of O positive blood including:

(1) normal donor criteria
(2) platelet count
(3) salicylate level

b. Draw one unit of blood from each donor.
c. Red cells and other components to be used routinely by the Blood Bank.
d. Preparation of platelets for freezing in accordance with the Dayian and Rowe procedure.
e. Aliquot each prepared platelet pack to be used as control and for testing.
f. Thaw platelets after 36 hours by submersion in a 40°C water bath with mild agitation for 20 seconds.
g. Sample control and test for bacteriologic control. Culture by the automated bacterial detection method on blood agar and peptone broth.
h. Test both test and control samples for platelet count, and osmolality of platelet concentration.

Phase II.

a. Screen 20 healthy routine blood donors of O positive blood including:

(1) normal donor criteria
(2) platelet count
(3) partial thromboplastin time
(4) salicylate level

b. Draw one unit of blood. Red cells and other components minus PRP to be used routinely by blood bank.
c. Preparation of platelets for freezing (see #4 through #7, Phase I.)
d. Test platelets, frozen and nonfrozen, for viability of recovered platelets in accordance with criteria established by Dayian, G. and Rowe, A.W., Cryobiology 13:1-8, 1976.

(1) uptake of ^{14}C serotonin
(2) (a) ADP induced aggregation
(b) epinephrine induced aggregation
(c) collagen induced aggregation
(3) clot reaction
(4) response to hypotonic shock
(5) platelet recovery and size distribution
(6) osmolality of platelet concentration

PROGRESS

(77 10 - 78 09) The low glycerol method of Dayian and Rowe for the cryopreservation of human platelets as modified in our laboratory was performed. Two groups of 22 units each were thus prepared, frozen, and thawed with a mean platelet yield of 70% and 84% respectively. Minor morphologic changes in the frozen platelets were observed at both the light and electron microscopic levels with the majority of the frozen and thawed platelets remaining essentially intact ultrastructurally. The frozen platelets were evaluated by means of three in vitro tests of platelet function: clot retraction, hypotonic stress, and serotonin uptake. As compared with corresponding fresh platelet function, the frozen platelets produced a mean clot retraction of 96%, a mean reversal reaction to hypotonic stress of 38%, and a mean serotonin uptake of 93%. Comparison was made with the morphology and function of fresh and three-day old hospital platelets. Platelet yields and in vitro function as measured by serotonin uptake were compared with those of Dayian and Rowe.

Results of this study were presented at the Third Annual Meeting of the Society of Armed Forces Medical Laboratory Scientists and, by invitation, at the Advanced Component Seminar of the Haemonetics Research Institute. An abstract will appear in the Proceedings of the Advanced Componets Seminar, Haemonetics Research Institue (in press).

STATUS: (O)

TITLE: Zinc, Copper, Arginine, Carnitine and Total Proteolytic Enzyme Concentration in the Seminal Fluid of Infertile Patients

PRINCIPAL INVESTIGATOR: CPT Michael L. Smith, MSC

WORK UNIT NO: 77/76

TECHNICAL OBJECTIVE

To measure the concentration of several components in the semen of a population of fertile and infertile patients and to compare the values. This information will add to our understanding of the role of these elements and compounds in fertility and may help in the management of infertile patients. A finding of abnormal values may also yield diagnostic tests for specific fertility problems.

METHOD

Semen will be collected from at least thirty patients who have fathered a child and these patients will be considered fertile and used as controls. Samples will also be collected from 30 patients whose wives have had a favorable OB-GYN checkup, but the couple cannot conceive. These patients will constitute an infertile population. A sperm count, motility, volume, viscosity, and morphology will be established for each sample one hour after collection. The samples will be frozen at -70°C, and the zinc, copper, arginine, carnitine, and proteolytic enzyme concentration will be determined at a convenient time. When all data are collected, the mean values for the fertile group will be compared with those of the infertile group.

PROGRESS

(77 10 - 78 09) Seminal fluid zinc and proteolytic enzyme concentrations have been measured in 50 prevasectomy patients. These values will be compared with those of 50 infertile patients. Triplicate semens from 10 infertile patients have been collected and are ready for assay. The semen component, prolactin, is also being investigated.

A paper entitled "Comparison of Prolactin Levels in Human Semen" has been accepted for publication by the Journal of Endocrinology.

STATUS: (O)

TITLE: Polyamines as Chemical Markers of the Response of Patients Being Treated for Cancer

PRINCIPAL INVESTIGATOR: CPT Michael L. Smith, MSC

WORK UNIT NO: 78/25

TECHNICAL OBJECTIVE

Studies suggest that following urinary polyamine levels can be an effective way to monitor patients under treatment for cancer. Our objective is to obtain pre-, during, and post-treatment urinary polyamine levels on patients with various cancers undergoing various methods of treatment and to correlate these levels with the patient's progress.

METHOD

Patients: The population of patients will be all consenting cancer patients undergoing chemotherapy, surgery, or radiation therapy. The group will also include benign tumor patients undergoing surgery.

Sample Collection: 24-hour urines will be collected in plastic urine bags containing 10 ml of concentrated HCl. Chemotherapy patients: samples will be collected before treatment, between the first and second treatments, and 10-20 days after the second treatment. Surgery and radiation patients: samples will be collected before treatment, 3-7 days post treatment, and 10-20 days post treatment. Three samples will be collected from each patient and a determination of the creatinine performed. An aliquot will be frozen for polyamine analysis.

Assay: The assay method will be developed concomitantly with sample collections and will include overnight hydrolysis in HCl, extraction with butanol, separation of dansyl derivatives by thin layer chomatography, and individual quantitation by fluorescent densitometry.

Analysis of Results: Urinary polyamine levels will be charted for each patient to determine: if pretreatment levels are above normal; what the levels are during treatment; if the levels return to normal after treatment; and if the trends in the levels indicate effective treatment when compared with the clinical signs and follow-up of the patient.

Polyamines as Chemical Markers - Smith

PROGRESS

(78 03 - 78 09) A thin-layer chromatographic technique for assaying polyamines in urine has been developed and evaluated. A radioimmunoassay for spermine and spermidine, developed by the University of Oregon Medical School, Department of Pediatrics, is being used for serum measurements. Five departments at MAMC and one at Silas B. Hays Hospital are evaluating cancer patients and collecting samples for this study.

STATUS: (O)

TITLE: Polymethylmethacrylate, Self Curing Acrylic Cement, as a Stimulator of Cellular Immunity

PRINCIPAL INVESTIGATOR: COL Stephen R. Thomas, MC

WORK UNIT NO: 75/26

TECHNICAL OBJECTIVE

The main purpose of this project is to determine if component loosening after total hip replacement where bacterial involvement is not indicated is, in fact, a cellular immune response (tissue rejection phenomenon).

METHOD

Phase I - Guinea pig stimulation phase in an attempt to promote an immune reaction. Procedure as outlined in protocol.

Phase II - Peripheral blood from two groups of humans will be collected. Group I will be those individuals who have never experienced any surgical procedure which required the use of methylmethacrylate (control group). Group II will be those individuals who have experienced any surgical procedure which required the installation of methylmethacrylate cement.

Ancillary Investigative Procedures - Sheep RBC properly treated as well as polystyrene latex particles could be employed to demonstrate the probable humoral antibody response. Potential development of a microagglutination procedure is feasible.

PROGRESS

(77 10 - 78 09) Samples have been taken from approximately 35 patients. Investigators are now ready to begin taking the second samples from these patients. COL Thomas is now stationed at Letterman AMC and is attempting to set up a branch of the study there. CPT William A. Bulley, Orthopedic Service, and James Graves, Clinical Investigation Service, are continuing the study at MAMC.

STATUS: (O)

TITLE: Effect of Chronic Oral Propranolol on Glucose Tolerance

PRINCIPAL INVESTIGATOR: MAJ Gary L. Treece, MC

WORK UNIT NO: 76/26

TECHNICAL OBJECTIVE

To determine what effect propranolol given orally for the treatment of hypertension and angina pectorus has on intravenous and oral glucose tolerance tests in light of recent case reports of hyperglycemia nonketotic coma attributed to propranolol therapy.

METHOD

Patients will be obtained by referral from Madigan Army Medical Center's Cardiology and Endocrinology Clinics where it will be determined that these patients require treatment with outpatient oral propranolol for hypertension, angina pectorus or control of arrhythmias. Patients with a history of bronchial asthma or congestive heart failure will be excluded from the study as well as patients with emphysema and insulin-dependent diabetes mellitus.

It is proposed that 30 such patients will voluntarily be submitted to an intravenous GTT and a three-hour oral GTT before and after two and six weeks of oral propranolol alone, and four weeks after propranolol and hydrochlorothiazide in combination (ten weeks after institution of propranolol). Patients will have ingested at least 150 gm of carbohydrate for three days prior to any GTT. Patients will be NPO after 2400 hours the evening before the day of any GTT. Other nonessential medications will be discontinued three days prior to any GTT. Doses of propranolol to be used will be 40 mg, q.i.d. (p.o.).

Effect of Chronic Oral Propranolol - Treece

PROGRESS

(77 10 - 78 09) No further progress was made on this protocol during the past year. Although it is expected that the study will yield negative results in that the results to date show no consistent abnormality of glucose tolerance with propranolol therapy, it is felt that such a report should be documented in the medical literature.

This protocol has been terminated at Madigan Army Medical Center and reinitiated at Fitzsimons Army Medical Center where MAJ Treece will continue the investigation.

STATUS: (T)

TITLE: Development of Teaching Models for Microvascular Anastomosis, Microneural Reconstruction and Tissue Reimplantation

PRINCIPAL INVESTIGATOR: MAJ George S. Ward, VC

WORK UNIT NO: 78/11

TECHNICAL OBJECTIVE

To develop teaching models for instruction and perfection of residents or staff in the field of microsurgery.

METHOD

Different species of laboratory animals and anatomical areas would be evaluated to determine which offer the least technical difficulties. Those models which are most successful would then be perfected for end to end and end to side arterial anastomosis. If interest and demand continue, models for microneural reconstruction and tissue reimplantation would also be developed. Various steps would be documented with photography. Contrast radiography would be used to demonstrate vascular patency.

The models developed under this protocol would be used to familiarize residents or other personnel with microsurgical techniques or to refresh staff proficiency prior to clinical application.

PROGRESS

(77 12 - 78 09) Work on this protocol has centered primarily around development and usage of models for microvascular anastomosis and training personnel in the microvascular technique. Staff members from various services, including Otolaryngology, Neurosurgery, Urology, Plastic Surgery, and OB GYN, have completed 77 microsurgical procedures. Carotid artery end-to-end and end-to-side anastomoses in guinea pigs and Sprague Dawley rats have been the models used most frequently. Venous anastomosis was practiced on young guinea pig jugular veins. In addition, oviducts from sheep and rabbits have been harvested for anastomosis procedures, and penile reattachment has been attempted.

STATUS: (O)

TITLE: A Radiological Study of Mechanically Produced Lesions in Human Mandibles

PRINCIPAL INVESTIGATOR: MAJ George H. Deitrick, DC

WORK UNIT NO: 78/23

TECHNICAL OBJECTIVE

To observe the location and amount of destruction necessary for a lesion in a human mandible to be detectable by dental radiography and to compare results using dry specimens and cadaver mandibles with soft tissue.

METHOD

Pre-operative photographs and radiographs of mandibles from cadavers; buccal-lingual block sections of mandibles: molar, bicuspid, anterior. Photograph and radiograph each section.

Create periodontal lesions with a #4 round bur; radiograph and photograph interproximal; buccal; lingual; furcation.

Create central bone lesions within block section; radiograph and photograph; remove cancellous bone only; remove buccal-cancellous cortex junction; remove lingual cancellous cortex junction.

Create periapical lesions with a #4 and #8 round bur; radiograph and photograph; extract tooth, create lesion, replace tooth.

Create external lesions with a #8 round bur; radiograph and photograph; 1 mm into buccal plate; ½ way through buccal plate; completely through buccal plate; same for lingual.

PROGRESS

(77 12 - 78 09) Six juvenile and four adult mandibles have been purchased with research funds. Four cadaver mandibles have been procured from the University of Washington. All other instruments and supplies have been assembled.

Experimentation has begun on producing lesions within the mandibles and radiographing the sites. The study is being documented with photographs. Expected completion date is December 1978. A manuscript should be ready for submission by March 1979.

STATUS: (O)

TITLE: Ultraviolet Photography as a Diagnostic Technique in Detecting Carcinoma

PRINCIPAL INVESTIGATOR: MAJ Richard L. Ferguson, DC

WORK UNIT NO: 77/85

TECHNICAL OBJECTIVE

To test a recently reported photographic phenomenon (Goldstein, N, et al: Ultraviolet Photography Skin Cancer Diagnosis and Other Clinical Applications. Functional Photography 12:34-37, 1977) for suitability as a reliable, cost effective diagnostic technique.

METHOD

A two-phase inquiry is planned. The initial part of the plan will deal with attempts to utilize low cost equipment to secure variable ultraviolet return and record comparison exposures on ordinary panchromatic emulsions (Kodak Tri-X). Results will be evaluated and a decision made as to proceed with the second phase. The second phase will reproduce the work of Goldstein, utilizing experimental controls and a statistical base. A third phase, assuming a high degree of success in phases I and II, would involve the formulation of an actual clinical diagnostic standard and submission of such a technique for field testing.

PROGRESS

(77 10 - 78 09) Phase I has been completed and one subject has been studied. Availability of patients who meet the criteria is proving to be a problem.

STATUS: (O)

TITLE: Periapical Healing Potential in Canals Obturated with Gutta Percha versus Silver Cones

PRINCIPAL INVESTIGATOR: MAJ William H. Fowler, DC

WORK UNIT NO: 76/14

TECHNICAL OBJECTIVE

The purpose of this investigation is to compare the periapical healing following instrumentation and obturation, short of the anatomical apex, with gutta percha to periapical healing following instrumentation and obturation, short of the anatomical apex, with silver cones.

METHOD

Eighteen noncarious, nonperiodontally involved monkey teeth were used in this study. The involved teeth were isolated with a rubber dam, and an aseptic technique commonly employed by endodontists was followed.

Following pulp extirpation and instrumentation short of the apex, six teeth were obturated with gutta percha, six teeth were obturated with silver cones, and six teeth served as a control and had no obturating material in the canal system. The latter were sealed from the oral environment with amalgam and copalite. Surgical block sections of the periapical region were taken after four months. Histologic examination will be used to determine the status of the periapical tissues.

PROGRESS

(77 10 - 78 08) Block sections from the experimental and control periapical areas were obtained and submitted to the pathology laboratory (USAIDR) for decalcification, serial sectioning, staining, and mounting. Microscopic evaluation of the serial sections revealed that laboratory processing had destroyed the relationship between the apices and the periapical tissues, making interpretation of the experimental results impossible. Therefore, the project has been terminated.

STATUS: (T)

TITLE: The Use of Fluoride and Custom Trays to Treat Dental Hypersensitivity Away From the Dental Office

PRINCIPAL INVESTIGATOR: MAJ Kjeld V. Hansen, U.S.A.F.

WORK UNIT NO: 78/19

TECHNICAL OBJECTIVE

To determine the effectiveness of the utilization of custom trays and a fluoride gel to eliminate or decrease dental hypersensitivity, especailly after periodontal surgery, and to evaluate this method for possible future self-treatment by the patient.

METHOD

Patients who have dental hypersensitivity after periodontal treatment will be screened to reflect surgery in opposite quadrants, either the maxilla or mandible. The patient's base pain threshold will be measured using a thermo-electric tooth stimulator invented by Dr. M. Ash of the University of Michigan, School of Dentistry, giving a baseline to measure from. The patient will have a custom tray (made of acrylic) fabricated to his specific oral anatomy of the teeth. Using the custom tray, dental personnel will apply a fluoride gel (strength 2.3%) to the tested site once a day for five minutes. The patient will be measured reference hypersensitivity and verbally questioned every week for one month. A 15 member group using a placebo and the above method will be used as a control. The findings will be accumulated and placed in a graphic/table form for analysis.

PROGRESS

(78 06 - 78 09) Patient selection is in progress. The power source has not been constructed due to a lack of funds.

STATUS: (O)

TITLE: The Effect of Abrasive Polishing Agents on Healing Periodontal Wounds

PRINCIPAL INVESTIGATOR: LTC William B. Hickman, DC

WORK UNIT NO: 78/27

TECHNICAL OBJECTIVE

It is widely held ture that meticulous professional cleaning of the teeth during the postsurgical phase of periodontal therapy is beneficial to the final surgical result; the use of tooth polishing compounds is a logical extension of this rationale. This project will evaluate the effect of these agents on a standardized periodontal wound in a suitable animal model system. Subcutaneous implant sites will also be done and examined for toxic results.

METHOD

Young adult Sprague-Dawley laboratory rats will be used in this study in the following manner:

Group I, Week I, 28 rats - the rats will receive, on their prepared backs, subcutaneous implants of the agents to be evaluated, e.g., flour of pumice, zircate, and zircate with SuF_2. A sham control site will also be placed on the back. Four standard intra-oral wounds will be created, and the same agents implanted, also with a control site. The rats will be sacrificed in groups of two at intervals of 1, 3, 6, 24, 48, 72, and 96 hours, and 5, 7, 9, 11, 14, 21, and 30 days after the operation, for gross and histologic examination. Representative sections of each area will be done by a gross evaluation of the wound healing site and microscopic examination under a high power field observing for neutrophilic infiltrate in the test areas that is in excess to that of the control site. A scoring method of infiltrate per high powered field will be used in order to achieve a quantitative result.

Group II, Week II, 28 rats - this group of rats will receive the standard intra-oral wound only with the implantation of the test substances, after which they will receive a standardized typical dental syringe washing of the test areas. A sham control site will be prepared. The animals will be sacrificed, sectioned, and prepared in a manner similar to Group I.

The Effect of Abrasive Polishing Agents - Hickman

PROGRESS

(78 02 - 78 09) All sections of the various phases of this study have been processed into slides for analysis. At present, the investigators are waiting for selected recuts of certain sections that were torn in the first processing. A rough draft of the study is expected by December and the final paper by April 1979.

STATUS: (O)

TITLE: The Use of Silastic as an Injectable Root Canal Obturating Material

PRINCIPAL INVESTIGATOR: MAJ Griffith B. Jones, DC

WORK UNIT NO: 77/12

TECHNICAL OBJECTIVE

To determine the clinical effectiveness of Silastic 382 Medical Grade Elastomer for root canal obliteration.

METHOD

Extracted human teeth will be prepared with an accepted endodontic technique and Silastic 382 Medical Grade Elastomer injected into the extracted teeth as the obturating material. The teeth will then be subjected to SEM analysis and tagged iodine to determine the effectiveness of its sealing properties.

PROGRESS

(77 09 - 78 01) This project has been completed. Silastic 382 mixed with 360 Medical Grade Fluid and barium sulfate was injected with a disposable tuberculin syringe and 25 gauge needle into the prepared root canals of 28 extracted human anterior teeth. Gutta percha with Proco-sol sealer obturated the seven control teeth. Autoradiography utilizing S^{35} was employed to determine the effectiveness of the apical seal. Both the experimental and control groups exhibited significant leakage, with the difference between the groups not being statistically significant.

A manuscript with the same title as the project has been submitted to the Journal of Endodontics for possible publication.

STATUS: (C)

TITLE: A Comparative Evaluation of the Relative Debriding Efficiency of the Type K and H Files Utilizing 5.25% or 1.00% Sodium Hypochlorite for Irrigation

PRINCIPAL INVESTIGATOR: MAJ W. Richard Liggett, DC

WORK UNIT NO: 76/10

TECHNICAL OBJECTIVE

The goal of endodontic therapy is to debride and completely obturate the pulp canal system. Since it is the desire of the practitioner to perform his therapy as effectively, efficiently, and with as little threat of toxicity to the patient as possible, the purpose of this study will be twofold. First, to study the relative ability of the Kerr file versus the Hedstrom file in debriding and smoothing the pulp canal wall, and, secondly, to see if there is any significant difference in canal cleanliness when utilizing a 5.25% or 1.00% solution of sodium hypochlorite as pulp canal irrigant.

METHOD

Forty-eight single-rooted extracted human teeth will be used. These teeth will be frozen as soon as possible following extraction and kept frozen until utilized in the experiment. The 48 teeth will be separated into three groups of 16 teeth, each. One-half of the teeth in each group will be instrumented with a series of Kerr files and the other half with Hedstrom files. Group I will be irrigated with a 5.25% solution of NaOCL; Group II will be irrigated with a 1.00% solution of NaOCL; Group III will be irrigated with saline which will serve as a control. The teeth will then be prepared for histologic examination and evaluation of the debrided and smoothed pulp canal wall.

PROGRESS

(77 10 - 78 09) Data are presently being analyzed. The results will be submitted to the Journal of Endodontics for publication.

STATUS: (O)

TITLE: Furcation Management I: Relationship of the Pulp Chamber to the External Aspect of the Furcation of Mandibular First and Second Molars

PRINCIPAL INVESTIGATOR: MAJ Philip Stanley, DC

WORK UNIT NO: 78/03

TECHNICAL OBJECTIVE

Before attempting an odontoplastic procedure, one should know the anatomical distance from the pulp chamber to the furcation. With this information, the dentist may remove sufficient tooth structure to eliminate an incipient lesion, yet not encroach on the pulp. The literature has many studies on dental measurements, yet to the knowledge of the principal investigator, there are no published dimensions in this area of interest. This will be the objective of this study.

METHOD

This study will measure the thickness of tooth structure from the pulp chamber to three points on the buccal and lingual surfaces of human mandibular first and second molars. The three points will be the CEJ, a point 1 mm into the furcation, and a third point one-half the distance from the CEJ to the measured point in the furcation. The measurement points will be determined by the use of a wax profiling apparatus that enables measurements made in a bucco-lingual plane from a fixed reference point to be related to a curved surface. Fifty molars will be selected from teeth extracted by the Oral Surgery Service and divided into three age groups: 18-25, 26-35, and 35 years plus.

A large occlusal endodontic opening with removal of the entire pulpal roof will be made. A spring loaded caliper will be introduced through the opening and measurements to within 0.1 mm will be taken.

The mean thickness to each external landmark in each age group will be computed. A comparison of the data among different age groups, using a student's t test, will be made to determine the effects of aging on the thickness of tooth structure in this area.

The results will be compared to Goldman's assertion (J Periodontology 29:112, 1958) that one millimeter may be removed without damage to the pulp's contents. Information from this study will be used to develop rational applications of odontoplasty to the treatment of periodontal lesions.

PROGRESS

(77/10 - 78 03) This project has been completed. The thickness of 39 mandibular molars subclassed by type and age was studied to determine if the dentin in the region of the root trunk was thick enough to permit an odontoplastic procedure and yet remain within the 2 mm guideline. An individual acrylic template and graph paper made it possible to locate and mark three related landmarks on each tooth surface. The minimum dentin thickness from each of these points to the pulp chamber was measured with a spring caliper to 0.1 mm. Comparison of the mean measurements and statistical analysis of the data led to the conclusion that odontoplasty in the region of the furcation or root trunk of mandibular molars may jeopardize the health of the dental pulp when used as an adjunct to pocket elimination.

A manuscript is now in preparation for possible publication.

The results of this study were presented at the University of Washington, Center for Research in Oral Biology Annual Research Conference, Seattle, WA, 12 June 1978.

STATUS: (C)

TITLE: The Immediate Sealing Properties of Cavit

PRINCIPAL INVESTIGATOR: MAJ Maylon J. Todd, DC

WORK UNIT NO: 76/09

TECHNICAL OBJECTIVE

Temporary filling materials are used in endodontics to seal the access cavity between treatments. The purpose of this study is to investigate the immediate sealing ability of Cavit.

METHOD

Eighteen extracted human teeth were separated into three groups, each containing six teeth. Access openings were prepared and sealed with Cavit. Group I teeth were immediately immersed in an S^{35} radioisotope solution. Group II teeth were placed in the isotope solution after a five-minute period to allow for maturation of the Cavit restoration. Group III teeth were immersed in the isotope solution after a 15-minute maturation period. After 24 hours in the isotope solution, a central longitudinal section (300 micrometers in thickness) was made from each tooth with a Bronwill thin-sectioning machine. From these central sections, autoradiographs were made and the level of isotope penetration determined.

PROGRESS

(77 10 - 78 09) Data are presently being analyzed. Findings will be submitted to the Journal of Endodontics for publication.

STATUS: (O)

TITLE: The Effect of Root Resection on the Apical Seal

PRINCIPAL INVESTIGATOR: MAJ Maylon J. Todd, DC

WORK UNIT NO: 76/13

TECHNICAL OBJECTIVE

The purpose of this study is to determine if root resection affects the integrity of the apical seal of previously obturated canals.

METHOD

Twenty-four extracted single-rooted human teeth were used in this study. Twelve teeth were obturated with gutta percha and sealer, and twelve teeth were obturated with silver points and sealer. Six teeth with each type of obturating material were subjected to the root resection procedure, using a high-speed handpiece and straight-fissure bur. The remaining twelve teeth were not resected and served as controls.

All teeth were placed in a S^{35} radioisotope solution for twenty-four hours. A central longitudinal section was made from each tooth with a Bronwill thin-sectioning machine. From these central sections, autoradiographs were made and the level of isotope penetration determined.

PROGRESS

(77 10 - 78 09) Data are presently being analyzed. Findings will be submitted to the Journal of Endodontics for publication.

STATUS: (O)

TITLE: A Clinical Determination of the Effectiveness of Endodontic Chemomechanical Sterilization

PRINCIPAL INVESTIGATOR: COL David R. Zielke, DC

WORK UNIT NO: 75/22

TECHNICAL OBJECTIVE

The objective of this study is to evaluate the efficacy of an accepted root canal preparation technique in producing sterilization of the root canal system.

METHOD

The plan is to endodontically treat single-rooted asymptomatic teeth that have roentgenographic evidence of periapical pathosis. All teeth will be isolated with a rubber dam and a conventional access preparation made. Two microbiological samples from each canal system will be made prior to instrumentation and at the completion of instrumentation. One will be incubated in prereduced sterilized medium and the other in trypticase soy broth with 0.1% agar as the control Canal preparation will now be completed in a conventional manner.

At each subsequent appointment, two additional microbiological samples will be obtained before and after instrumentation. All canals will be obturated by the lateral condensation of gutta percha and sealer.

The patients will be reexamined at 6 and 12 month intervals. Another roentgenograph will be made. They will be placed in success or failure categories as defined by Storms. The findings will be correlated with the culture results.

PROGRESS

(77 10 - 78 10) Sixty-one single-rooted teeth were treated to determine the sensitivity of non-rereduced PRS medium and to compare it to the sensitivity of TSB in the detection of microorganisms from the root canal. Results demonstrated that a seven-day incubation period is required for an accurate determination of the results.

A Clinical Determination - Zielke

Earlier studies had a culture reversal rate of 48.5%, indicating that aerobic and anaerobic culturing are an extremely unreliable sample.

Results showed the use of non-rereduced PRS medium was not as sensitive as rereduced PRS and offers no significant advantages over TSB in endodontic culturing.

One paper has previously been published on the early results of this study (Annaul Report FY 77), and a new paper entitled "An Analysis of the Sensitivity of Non-Rereduced PRS Medium in Endodontic Therapy" has been submitted for publication.

STATUS: (O)

TITLE: Hypertension in Children and Youth and Family Profile of Hypertension

PRINCIPAL INVESTIGATOR: CPT Douglas L. Attig, MC

WORK UNIT NO: 77/09

TECHNICAL OBJECTIVE

To identify all Family Practice Clinic patients who meet the following criteria:

1. Are under the age of 18 years.
2. Whose systolic and/or diastolic blood pressures fall above two standard deviations of the mean of the general population by commonly accepted criteria.
3. Are expected to remain in the area for the next full year.

Analyses of age and race distribution and familial aggregation of hypertension will be made. Special studies on those patients with persistent hypertension will be done at a later date.

METHOD

All patients under the age of 18 who are seen in the Family Practice Clinic will have their blood pressures taken by nursing personnel. Family physicians will examine the blood pressure values according to criteria for the study. A computerized listing of all Family Practice patients with diagnoses of uncomplicated hypertension, labile hypertension, hypertension with target organ involvement or hypertension NOS will be obtained. Those patients with children under the age of 18 will receive a form letter describing the study and requesting them to make arrangements to have their children screened at the clinic.

PROGRESS

(77 10 - 78 08) In the prior year 500 children were screened on routine physical exam and approximately 10% had BP higher than the standard deviation. Because of this a mass screening program was to be developed for use in the clinic. Further studies revealed no meaningful data and the protocol was terminated for lack of support from the staff.

STATUS: (T)

TITLE: The Doctor-Patient Relationship: Critical Elements. A Questionnaire to Identify Pivotal Physician Qualities and Help Individual Physicians Improve Interaction with Patients.

PRINCIPAL INVESTIGATOR: CPT Thomas H. Auer, MC

WORK UNIT NO: 78/24

TECHNICAL OBJECTIVE

1. To offer each senior resident and staff family doctor a confidential profile of himself as seen by his patients.

2. To define and identify those elements of the doctor-patient relationship that contribute most to its strength or weakness.

3. To compare the doctor's global impression of his patient-interaction to the patient's perception of that interaction, and to identify specific qualities or behavior exhibited by the doctor in his office which are misperceived by the patient.

METHOD

A short simple questionnaire has been designed to be answered by the patient for evaluating his doctor on multiple factors felt necessary to reflect a good doctor-patient interaction. The questions address separate aspects of this interaction and allow the patient to comprehensively evaluate his physician. The physician can likewise fill out the same questionnaire using what he sees as his own global impression being presented by him to his patients. Patient participants must be at least 13 years of age and have been seen twice by the physician. The privacy of the physicians will be maintained through a coding system. The results of the questionnaires will be analyzed, and a correlation will be made between the physician's answers and his patient's answers.

PROGRESS

(78 01 - 78 09) The technical aspects of this project have been completed and statistical analysis is complete. A manuscript is in preparation.

Presentation: The Doctor-Patient Relationship: Critical Elements

The Doctor-Patient Relationship: Critical Elements - Auer

Presented to: University of Washington Family Practice Residency Network Meeting, Seattle, WA, April 1978.

Uniformed Services Chapter of the American Academy of Family Practice Annual Meeting, Jacksonville, Florida, April 1978.

STATUS: (C)

TITLE: Early Detection and Prevention of Thrombophlebitis

PRINCIPAL INVESTIGATOR: MAJ Henry D. Covelli, MC

WORK UNIT NO: 77/50

TECHNICAL OBJECTIVE

The incidence of thrombophlebitis in bedridden or post-operative patients approaches 20-40% when sensitive diagnostic techniques to detect venous thrombosis are utilized. Since pulmonary emboli originate from these lesions, many investigators have recommended prophylactic anticoagulation for all high risk patients. The purpose of this study is to further define these high risk groups by use of radioiodinated fibrinogen, venous Doppler exam and hypercoagulable screening tests. Concurrently, the utility of thromboembolic disease (TED) stockings would be determined by randomly allocating a TED stocking to only one leg, thereby allowing each patient to serve as his own control.

METHOD

A group of patients at high risk for developing thrombophlebitis would undergo fibrinogen scanning. Abbott Laboratory is the only source of FDA approved 125 I fibrinogen. Their protocol will be followed:

1. Blockade of the thyroid gland to prevent uptake of 125 I.
2. Intravenous administration of less than 140 µci 125 I fibrogen.
3. Scintillation counting at the bedside.

This group of patients would receive, by random allocation, a TED stocking on either right or left leg, to be worn for approximately one week while being studied. This group would include: elderly patients undergoing major surgical procedures, elderly patients with suspected myocardial infarcts and bedridden patients undergoing prolonged hospitalization. On admission, an extra blood sample would be drawn with routine studies for measurement of antithrombin III levels. Venous Doppler exam and venogram would only be done if clinically indicated.

Early Detection and Prevention of Thrombophlebitis - Covelli

PROGRESS

(77 10 - 78 09) Due to the poor results of positive tests with our I_{131} fibrinogen, even in venogram positive patients, the investigators did not embark on the study of the early detection of thrombophlebitis, and the project was terminated.

STATUS: (T)

TITLE: Immunological Mechanism of Gold Hypersensitivity

PRINCIPAL INVESTIGATOR: MAJ Henry D. Covelli, MC

WORK UNIT NO: 77/79

TECHNICAL OBJECTIVE

Approximately 50 patients receive gold therapy in Rheumatology Clinic in any one year. The frequency of side effects causing cessation of this therapy is approximately 25%. Many of these reactions will not persist if gold therapy is restarted; however, the morbidity to those patients that are rechallenged may be significant. Therefore, it is important to define this population. Lymphocyte transformation tests have been used to determine patients' idiosyncratic reactions to various drugs, including gold; however, with conflicting results. The purpose of this study will be to define those patients who would develop delayed hypersensitivity reactions to gold. More importantly, it will help define those patients who should not be rechallenged with gold after initial cessation of therapy because of a hematologic, renal, or integumentary reaction.

METHOD

Approximately 15 cc of blood will be obtained by venipuncture from patients with seropositive rheumatoid arthritis who have been started on gold therapy or have previously been exposed to gold therapy which had to be discontinued due to side effects. These venous samples will be used to perform in vitro lymphocyte transformation to PHA and gold and serum IgE levels.

PROGRESS

(77 10 - 78 08) After assessing results in seven patients with gold hypersensitivity type reactions, none had positive in vitro stimulation. Either our assay was not functional or we were not appropriately choosing a good patient population. The protocol has been terminated.

STATUS: (T)

TITLE: Determination of Normal Range for Six-Hour Radioactive Iodine Uptake Using 123 Iodine in Order to Eliminate Need for Most 24-Hour RAIU

PRINCIPAL INVESTIGATOR: LTC John L. Espinosa, MC

WORK UNIT NO: 77/56

TECHNICAL OBJECTIVE

123 iodine is a recently available radionuclide of iodine. Its physical properties make it far superior to the presently used 131 iodine for thyroid imaging and uptake. There is a 20-100 fold decrease in radiation to the patient using 123 iodine rather than 131 iodine. With 123 iodine the scan and uptake can be performed six hour after dosing, while with 131 iodine, uptake and scan is usually performed 24 hours after dosing, requiring appointments on two consecutive days. The normal 6-hour uptake with 123 iodine is unknown. We plan to determine the normal range for 6-hour uptake using 123 iodine and compare this with the 24-hour uptake. When this normal range is known, most 24 hour uptakes will not be necessary.

METHOD

Patients who have had a routine thyroid uptake or scan ordered by physicians other than those involved in the investigation will be screened for adequacy of inclusion into the study. Informed consent will be obtained on all patients. Many thyroid uptakes and scans are ordered in patients who do not have thyroid disease, e.g., patients with past history of head and neck irradiation, patients with thyroglossal duct cysts, and patients with cervical lymphadenopathy. These would be suitable patients for the study. All patients must be diagnosed as either euthyroid, hyperthyroid or hypothyroid by clinical evaluation and the following laboratory tests: T3 uptake, T4 by RIA, T3 by RIA, thyroid and microsomial antibodies. One of the three investigators will evaluate each of the patients to rule out thyroid disease. A dose of from 300 to 400 uCi of 123 iodine will be administered to the patient orally. Radioactive iodine uptake will be determined at 6 and 24 hours. A thyroid image will be performed six hours following dosing. This will decrease irradiation to the patient's thyroid from approximately 100 rads using 131 iodine to 2-3 rads using 123 iodine.

Determination of Normal Range for Six Hour RIAU - Espinosa

Those patients who are clinically and chemically euthyroid will be evaluated to determine the normal range of thyroid uptake of 123 iodine at 6 hours, and this will be compared to their 24-hour uptake. It is anticipated that a range of normals can be determined at 6 hours which will exclude all hypo and hyperthyroid patients. In a few patients who have borderline low or high 6-hour uptakes, a 24-hour uptake will have to be determined. From evaluation of the chemical data, a normal range for T3 uptake, T4 by RIA, T3 by RIA, and TSH will be determined. It is anticipated that approximately 100 patients should be evaluated to obtain reliable statistical information. At four patients per week, this will take approximately 6 months.

PROGRESS

(77 10 - 78 09) This protocol has been terminated due to a lack of sufficient data for meaningful results and due to the departure of the principle investigator and a professional assistant.

STATUS: (T)

TITLE: Development of Radionuclide Angiocardiography as a Clinical Diagnostic Tool for the Quantification of Left to Right Cardiopulmonary Shunts

PRINCIPAL INVESTIGATOR: LTC John L. Espinosa, MC

WORK UNIT NO: 77/57

TECHNICAL OBJECTIVE

The objective of this project is the local development of an existing radionuclide angiocardiography technique to be used in the diagnosis and management of patients with left to right cardiopulmonary shunts. A correlation between results obtained by this technique and those obtained by oximetry during cardiac catheterization will be established and findings from this study will be published.

METHOD

Patients will be those who will undergo or who have recently undergone cardiac catheterization and whose clinical condition will allow them to be safely included in this project. Of these patients, some will be studied twice in order to correlate peripheral injection with injection through a pre-existing catheter. Patients undergoing other nuclear medicine procedures involving appropriate isotopes in which the immediate flow study is not of benefit will also be used.

Each study will be performed using procedures similar to a brain scan except that the camera will be positioned over the heart and lungs. The data base for each study is the quantized sequential time pictures of the distribution of radioactivity in the patient's heart and lungs. Entry to the venous system for the injection will be gained by peripheral venipuncture or through a preexisting catheter.

From the data base, a time versus activity curve will be generated for various regions of the lungs. This curve will then be mathematically analyzed to determine the ratio of pulmonary to systematic blood flow (Qp/Qs). Results from patient studies using the two methods of injection will be compared to establish the validity of the peripheral venipuncture. Finally, the pair of Qp/Qs ratios for each patient obtained by oximetry and by the radionuclide technique with peripheral injection will be statistically correlated.

Development of Radionuclide Angiocardiography - Espinosa

PROGRESS

(77 10 - 78 08) The clinical utility of nuclear cardiology diagnostic procedures in the evaluation of left-to-right and right-to-left shunts, ventricular function, and cardiac mal-positions as well as differential pulmonary bloodflow has been adequately demonstrated at MAMC.

The findings of this protocol have resulted in two presentations to date and it has been accepted for two national meetings in the fall and winter.

The presentation entitled "The Role of Radionuclide Angiocardiography in Clinical Pediatrics" won the Andrew M. Margileth Award (best clinical paper presented by an active duty pediatrician) at the 13th Annual Uniformed Services Pediatric Seminar, San Francisco, 13-16 March 1978.

STATUS: (C)

TITLE: Diagnostic Utility of CSF Serologies and Rabbit Inoculation in Neurosyphilis

PRINCIPAL INVESTIGATOR: CPT Shannon M. Harrison

WORK UNIT NO: 77/93

TECHNICAL OBJECTIVE

To evaluate the diagnostic utility of cerebrospinal fluid VDRL, FTA, FTA-absorbed, and rabbit testicular inoculation with dark-field microscopic examination in the diagnosis of neurosyphilis.

The second purpose of this project is to determine if adequate cerebrospinal fluid levels of penicillin can be achieved on an outpatient treatment schedule.

METHOD

Twenty patients will be chosen in whom syphilis of more than one year's duration is suspected. After physical exam, LP will be performed for fluid for animal culture, cell count, glucose, protein, VDRL, and FTA-ABS and FTA-un ABS. CSF (0.5cc) will be injected into the testis of a young male rabbit with a control negative VDRL. Evidence of a positive culture will be taken by darkfield microscopy as demonstration of treponema in the injected testicle and not the control testicle.

One-half of the patients will be randomly selected for treatment with 2.4×10^6 units benzathine pen IM q. week x 3 as the CDC recommends and retapped 24 hours after the third dose. Penicillin levels will be measured and recorded. If the initial LP was positive for treponema, repeat injection will be carried out with a CSF specimen from three weeks post treatment.

One-half of the patients will be treated with 1.2×10^6 units procaine pen IM qd x 10 days. Repeat LP will be done 4 hours after tenth dose for a measurement of the penicillin levels. If the initial LP was positive for treponema, repeat injection will be carried out with a specimen from three weeks post treatment.

Diagnostic Utility of CSF Serologies and Rabbit Inoculation in Neurosyphilis - Harrison

PROGRESS

(78 03 - 78 09) Specimens have been obtained from three patients and are being stored. When more patients are available to obtain specimens from, all the levels will be run at one time.

STATUS: (O)

TITLE: Daunomycin Therapy in Acute Leukemia (Phase I)

PRINCIPAL INVESTIGATOR: LTC H. Irving Pierce, MC

WORK UNIT NO: 73/47

TECHNICAL OBJECTIVE

The purpose of this project is to institute the use of Daunomycin, a potent chemotherapeutic agent, as a second order drug in the treatment of acute childhood or adult leukemias for chemotherapeutic regimens.

METHOD

Daunomycin will be used for purposes of an induction and consolidation therapy in cases of acute childhood or adult leukemias or in those who have clearly relapsed on other drug regimens or patients not responding to such chemotherapeutic regimens as Vincristine and Prednisone, OAP, or the combination of Cytosine Arabinoside and 6-Thioguanine. Daunomycin will be given in one of the following three schedules depending on the type and extent of previous chemotherapy:

1. Daunomycin, 1-2 mg/kg IV every week

2. Daunomycin, 1 mg/kg IV x 5 days
   Vincristine, 2.0 mg IV on day 1
   Prednisone, 60 mg/day x 5 days po

3. Vincristine, 2.0 mg IV on day 1
   Prednisone, 25 mg qid po x 5 days
   Cytosine Arabinoside, 100 mg/M^2/day as continuous IV x 5 days
   Daunomycin, 60 mg/M^2 IV on day 1 only

The dosage and duration of therapy with Daunomycin and other combination drugs will be prorated according to the degree of response and bone marrow cellularity (as determined by weekly or bi-monthly marrow aspirates). Upon achievement of a complete remission, 2-3 additional courses of therapy will be given for purposes of consolidation, followed by maintenance therapy with other forms of drug agents.

Daunomycin Therapy in Acute Leukemia (Phase I) - Pierce

Prior to institution of therapy, an electrocardiogram will be obtained and also prior to subsequent courses of therapy. Peripheral blood counts will be performed 3 times weekly in all cases. Side effects such as myelotoxicity, nausea and vomiting following administration, skin rashes, alopecia, cardiotoxic effects such as congestive heart failure or cardiac arrhythmias, will be evaluated and noted in all patients placed on the drug.

PROGRESS

(77 10 - 78 01) One patient was treated on this protocol during this period. The patient was a 57 year-old male with a diagnosis of chronic myelocytic leukemia with blastic transformation. A total dose of 390 mg was given over a three-day period, resulting in severe myelosuppression and complete remission.

This protocol was terminated, and a new protocol was initiated with the same name and a different drug regimen.

STATUS: (T)

TITLE: Daunomycin Therapy in Acute Leukemia (Phase II)

PRINCIPAL INVESTIGATOR: LTC H. Irving Pierce, MC

WORK UNIT NO: 78/04

TECHNICAL OBJECTIVE

This is not a research study, but rather a treatment protocol involving an experimental drug. The objective is to continue the use of daunomycin in combination with other conventional chemotherapeutic agents for the treatment of leukemia as an extension of Phase I of the protocol, but with a different regimen of drugs.

METHOD

Duanomycin in combination with cytosine arabinoside, 6-thioguanine, vincristine, and prednisone will be given for seven days as remission induction treatment. A bone marrow sample will be obtained in 2-4 weeks; if evidence of the leukemia persists, a second induction course will be given. If leukemia cells are visibly absent, one to two additional courses will be given as consolidation therapy in an attempt to eliminate any residual leukemic cells. At that point, maintenance therapy will be provided. Dosage and duration of therapy are outlined in paragraph 6.0 of the protocol.

PROGRESS

(78 01 - 78 09) Two patients, both with a diagnosis of acute lymphocytic leukemia, have been treated on this protocol. Treatment for both patients resulted in severe myelosuppression and complete remission.

STATUS: (O)

TITLE: Cooperative Study for the Analysis of Risk Factors in Young Coronary Patients

PRINCIPAL INVESTIGATOR: COL James W. Reed, MC

WORK UNIT NO: 72/06

TECHNICAL OBJECTIVE

A unique opportunity exists in the Army to study a large group of young coronary patients by pooling together the case material of all the Class II hospitals. It is the purpose of this study to investigate these patients in comparison to age-matched controls for the following: obesity, hypertension, family history of coronary disease, plasma lipid classification, smoking history, carbohydrate intolerance, and insulin response to glucose load.

In the study of these parameters in young coronary patients, those factors of major importance in the development of coronary disease should be detected because they have caused the disease to manifest at a young age.

METHOD

All patients who develop proven coronary disease under the age of 40 who are patients at any of the Class II Army hospitals are subjects for the study. Age-matched individuals without coronary disease from the same institution will serve as controls. Patients and controls will be studied for the parameters as listed above.

PROGRESS

(77 10 - 78 09) Twenty-two patients have been studied. No more patients are to be entered and statistical evaluation of data is now in progress. A paper for submission for publication is now in preparation.

STATUS: (O)

TITLE: The Detection of Mental Aberration in Patients with Hypercalcemia and Response to Treatment

PRINCIPAL INVESTIGATOR: COL James W. Reed, MC

WORK UNIT NO: 76/30

TECHNICAL OBJECTIVE

The objective of this study is to quantitate the degree of mental aberration in hypercalcemia and to quantitate the response following treatment of the hypercalcemic state.

METHOD

All patients entered in the study must have chronic hypercalcemia and be a candidate for surgical treatment. This will be done by measurement of serum calcium and phosphorus x 5, serum chloride, serum PTH, urinary calcium and phosphorus, and TRP. Following an established diagnosis of hyperparathyroidism, multiphasic testing with the Minnesota Multiphasic Personality Inventory will be done by Department of Psychiatry under direction of Dr. Raymond Parker. Surgical exploration of neck will be performed by Dr. Praeger, Department of Surgery. At intervals of 2 weeks, 6 weeks, and 6 months, multiphasic testing will be repeated by Department of Psychiatry. Numerical quotients will be established for each test and degree of change will be established.

PROGRESS

(77 10 - 78 09) Twelve patients have been maintained to the completion of this study. They were studied with pre-op exams and two post-op exams (1 week post-op and 6 months post-op). Data is now being statistically analyzed in preparation for possible publication.

STATUS: (C)

TITLE: Performance Verification of A Lithium Powered Cardiac Pacemaker

PRINCIPAL INVESTIGATOR: MAJ Donald M. Rocklin, MC

WORK UNIT NO: 77/31

TECHNICAL OBJECTIVE

Cardiac pacemakers are recognized life prolonging devices for patients with excessively slow heart rates and uncontrollable ventricular arrhythmias. A major limitation in their utility, however, has been short battery life. When battery exhaustion occurs, a repeat surgical procedure and an entire new pacemaker generator system are necessary. Longer-lived power sources of greater energy density coupled with reliable components would help eliminate this problem in younger recipients.

An opportunity is available to participate in an ongoing performance verification protocol sponsored by Edwards Pacemaker Systems for a lithium powered pacemaker whose projected longevity is superior.

METHOD

This institution would be one of approximately forty medical centers participating in this study. Informed consent will be obtained from each appropriate candidate. Extensive implantation records and follow-up data, one to six months to end of pacemaker life, will be provided to Edwards Laboratories. They, in turn, will compile all data and publish an accumulated summary periodically.

PROGRESS

(78 01 - 78 08) This protocol was never implemented due to a one year delay in obtaining approval from OTSG. The pacemaker was studied and market approved by the F.D.A.

STATUS: (T)

TITLE: In vitro Identification of Tumor Associated Antigens

PRINCIPAL INVESTIGATOR: COL Clarence M. Virtue, MC

WORK UNIT NO: 75/14

TECHNICAL OBJECTIVE

The purpose of this investigation is to identify, using an in vitro technique, the tumor associated antigens of breast carcinoma.

METHOD

Phase I: Ten C3H-strain mice with implanted murine breast carcinoma will be obtained, and, after tumor growth has progressed beyond palpable stage, the mice will be sacrificed, and tumor tissue removed. Tissue treatment as listed in protocol.

Phase II: Tumor tissue obtained from the Department of Pathology (either from autopsy or surgical specimen) and non-tumor tissue from the same subject will be emulsified and treated in a similar manner as the mouse tumor tissue outlined in Phase I.

Phase III: Once the specific tumor associated antigens from mouse breast carcinoma are separated (Phase I), the antigens will be pooled and held at -80°C. Forty C3H-strain mice with implanted murine breast carcinoma will be obtained. Ten of these mice will be separated and have no further procedures. Twenty other mice will undergo resection of the tumor mass, and ten will subsequently receive an injection of the specific murine tumor associated antigens (obtained in Phase I) combined with Fruend adjuvant, followed by a booster injection with tumor associated antigen without tumor resection. The mice will then be observed and compared.

PROGRESS

(77 10 - 78 09) Breast carcinoma tissue homogenized in saline, centrifuged, and supernatant concentrated. Protein separated by G-200 column. Fractions concentrated and aliquots used in PHA lymphocyte stimulation. G-200 first peak separation fraction produced suppression of PHA lymphocyte stimulation. Further clarification of this response awaits further fractionation.

STATUS: (O)

TITLE: Serum RAST Titer Changes in Allergic Patients on Desensitization and the Correlation with Skin Test Changes

PRINCIPAL INVESTIGATOR: COL Clarence M. Virtue, MC

WORK UNIT NO: 77/67

TECHNICAL OBJECTIVE

To study the changes in serum IgE reagenic antibody at various times during desensitization and compare these changes with the clinical course and skin test results.

METHOD

Patients seen by the Allergy Service will be given the usual allergy evaluation to include clinical history, physical examination, appropriate skin tests, laboratory blood tests and pulmonary function spirometry. A 5 cc aliquot of serum will be reserved and tested for specific IgE reagenic antibody titers by the RAST technique, performed by the Nuclear Medicine Service. Those patients who are placed on densitization treatment will be reevaluated at appropriate intervals by the Allergy Service, at which time serum will again be drawn for repeat RAST titers and compared with skin test results and correlated with the clinical course.

PROGRESS

(77 10 - 78 09) Initial RAST titers to various pollens obtained. Patients then placed on desensitization immunotherapy. One year later repeat RAST titers obtained. This will be repeated after another one year interval.

STATUS: (O)

TITLE: Immunotherapy of Murine Mammary Carcinoma

PRINCIPAL INVESTIGATOR: COL Clarence M. Virtue, MC

WORK UNIT NO: 77/77

TECHNICAL OBJECTIVE

Immunotherapy has as yet made only a minimal contribution to the treatment of malignant disease, due in large measure to the lack of pure tumor associated antigen. If tumor associated antigen were obtained in pure form and administered with Levamisol so as to enhance the anti-tumor immune response, after surgery and chemotherapy had reduced tumor load, results might be markedly improved. The purpose of this protocol is to explore that possibility, using mammary tumor-bearing mice.

METHOD

Murine mammary tumors from tumor-bearing mice will be excised, the tumor tissue homogenized in saline and freeze-thawed, and the supernatant concentrated by dialysis against dry silica gel and passed through G-200 sephadex column for separation. The separate fractions so obtained will then be concentrated and small aliquots of each fraction will be tested for tumor antigen by skin testing on the mice whose tumors have been excised. Fractions identified as having tumor associated antigens will then be processed by quantitative electrophoresis to separate the individual proteins. These individual fractions will be concentrated and the fraction containing tumor antigen will be identified by skin testing on tumor-excised mice. After identification of specific tumor antigen fractions, more will be separated from additional tumor and used to treat various groups of mice as outlined in the protocol. All groups of mice will be compared for length of survival.

PROGRESS

(77 10 - 78 09) Tumor line begun from seed-mice and continued in C_3H mice bred in colony. Tumor harvested and homogenized in saline. Attempt at G-200 column separation resulted in loss. This is to be attempted again.

STATUS: (O)

AD-A068 421 MADIGAN ARMY MEDICAL CENTER TACOMA WASH F/G 6/5
CLINICAL INVESTIGATION SERVICE ANNUAL RESEARCH PROGRESS REPORT,--ETC(U)
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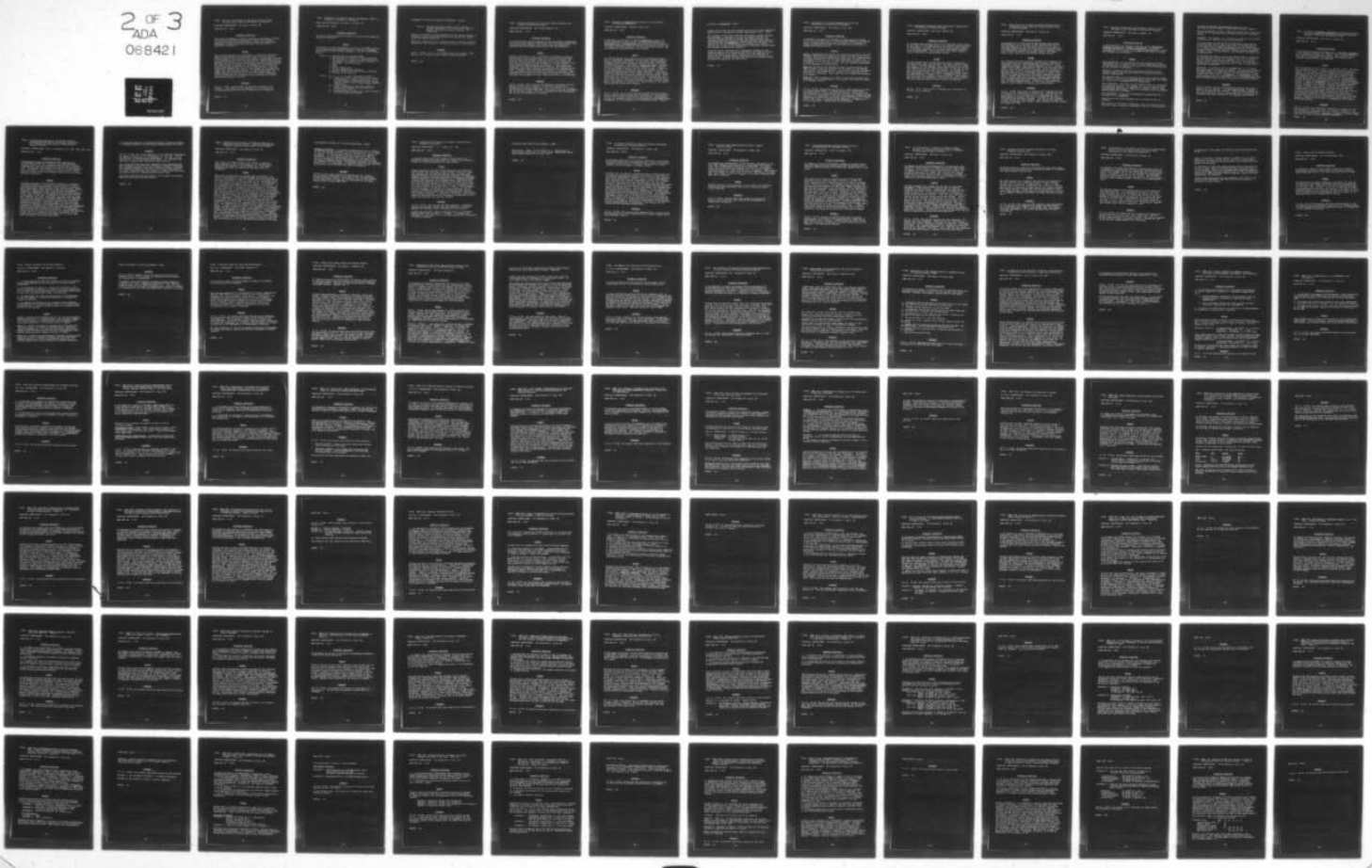

TITLE: The Work of Breathing on Continuous Positive Airway Pressure versus Positive End-Expiratory Pressure

PRINCIPAL INVESTIGATOR: MAJ Barry J. Weled, MC

WORK UNIT NO: 78/40

TECHNICAL OBJECTIVE

This study is designed to evaluate the work of breathing involved in continuous positive airway pressure versus positive end-expiratory pressure and to determine if there is a significant difference in oxygen consumption between these two modes of mechanical ventilation.

METHOD

Ten to twenty patients with hypoxemia on a mechanical ventilator requiring end-expiratory pressure will have flow and pressure monitors which do not interfere with mechanical ventilation inserted in the mechanical ventilator delivery system. Measurements will be made while the patient is on five minutes of positive end-expiratory pressure and on five minutes of continuous positive airway pressure. Two trials (order of trials will be randomized) of each mode of pressurizing ventilation will be run on each patient. The flow sensor will integrate the flow to tidal volume, and the pressure sensor will record airway pressure. A respiratory integrator will combine flow and volume and obtain the work of breathing. An oxygen analyzer will be placed in line, and oxygen consumption will be calculated for the various trials utilizing the volume measurements referred to above.

PROGRESS

(78 05 - 78 09) The equipment has not been available until recently. The checkout of the equipment is in progress, but is being delayed until electrical renovations are completed.

STATUS: (O)

TITLE: Management of Premature Rupture of Membranes (PROM) in Patients at 36 Weeks (+) Gestation

PRINCIPAL INVESTIGATOR: CPT Kevin C. Kelley, MC

WORK UNIT NO: 78/26

TECHNICAL OBJECTIVE

To assess fetal and maternal outcome in patients with premature rupture of membranes.

METHOD

To determine the best management in patients with PROM utilizing either pitocin augmentation/induction or expectant management, the subjects will be randomly assigned to one of the following groups:

Group A:
1. Speculum exam to establish PROM
2. Endocervical C&S aerobic by sterile speculum
3. OB examination - Leopold to establish position and vaginal to establish station, dilation, effacement, and Bishop score.
4. Prep
5. Enema
6. Hourly temperatures
7. Pitocin augmentation/induction
8. External and internal monitoring as indicated
9. Delivery by OB criteria

Group B:
#'s 1, 2, 3, 4, 6, and 9 the same as Group A.
#5 - enema only after clinical criteria for labor established by 5 minute contractions x 1^{o} on external monitor accompanied by pain, nausea, vomiting, need to push, bloody show/or further bloody show.
#7 - pitocin augmentation only after definite evidence of hypotonic uterine inertia in active phase at Cx C/5.
#8 - External monitoring only until other criteria for active phase established.

Management of Premature Rupture of Membranes - Kelley

Group C: The same as Group B except that no digital vaginal examination will be done until definite evidence of labor by clinical criteria is established.

Rupture of membranes will be assessed by gross vaginal pooling of fluid per os or by both nitrazene positive and positive examination of vaginal secretions.

Duration of gestation will be assessed based on history, physical examination, and laboratory results as outlined in the protocol.

PROGRESS

(78 03 - 78 09) To date, two patients have been studied. The project will continue as more subjects become available.

STATUS: (O)

TITLE: Clinical Evaluation of the Roche Tissue pH Monitor for Intrapartum Fetal Monitoring

PRINCIPAL INVESTIGATOR: COL Joseph Sakakini, MC

WORK UNIT NO: 77/84

TECHNICAL OBJECTIVE

To ascertain the clinical accuracy of this new method of monitoring fetal pH in labor against simultaneous fetal capillary samples and cord blood pH at delivery, and to ascertain the incidence of maternal and fetal complications due to this new electrode.

METHOD

Patients considered to be at high risk for problems in labor as determined by the investigators will be counseled and the appropriate consent form signed. When the cervix is at least 4 cm dilated, the electrode will be placed on the fetal presenting part after the patient has been prepped in a sterile manner. The Roche tissue pH electrode will be utilized in these cases and connected to a Roche Fetasonde Fetal Monitor. The uterine contractions, fetal heart rate and tissue pH will be recorded during labor. Periodic fetal capillary pH samples will be obtained as will cord blood pH (both arterial and venous) at delivery. These neonates will be observed in the nursery and again at 28 days to ascertain the incidence of fetal complications due to the pH probe.

PROGRESS

(78 02 - 78 08) This protocol was approved by the Human Subjects Research Review Board. However, the FDA had rescinded its permission for the investigational use of the monitor by the time the protocol was finally approved. The protocol has been terminated due to the FDA's action, but will be resubmitted when FDA approval for the use of the monitor is received.

STATUS: (T)

TITLE: Biotypes of Haemophilus Encountered in the Clinical Microbiology Laboratory

PRINCIPAL INVESTIGATOR: Andrew E. Back, DAC

WORK UNIT NO: 78/22

TECHNICAL OBJECTIVE

To determine the biotypes of various Haemophilus species that can be recovered in the clinical laboratory (principally H. influenzae and H. parainfluenzae) and correlate these biotypes with such factors as source of specimen from which isolated, age of patient from which isolated, the serotype of the isolate, and the antibiotic susceptibility of the isolate.

METHOD

The Minitek System, which employs substrate-impregnated paper discs to determine biochemical activity among various genera of bacteria and has proven useful in identifying other fastidious pathogens, was used in preliminary studies at MAMC and proved satisfactory for use in biotyping of Haemophilus spp. Selected strains, suspended in skim milk and frozen at -70°C, together with newly isolated strains, will be tested against a large number of substrates in the Minitek system for purposes of biotyping and determining the most useful substrates. Other tests routinely performed will be the oxidase reaction, susceptibility tests, test for beta-lactamase production and serotyping. Work cards have been retained for each isolate, containing the age of the patient and the source of each isolate. The following information will then be correlated: biotype, serotype, factor requirements, susceptibility to penicillin, age of patient, and source from which the strains were isolated.

PROGRESS

(77 12 - 78 09) As no funds could be provided for this project, only a somewhat limited study could be made by utilizing materiel on hand, not urgently required for other purposes, and preparation of our own media rather than purchasing the prepackaged media recommended by the manufacturer of the Minitek System. Control

studies showed that our media worked just as well as the commercial media and at a considerable savings (approximately $200 - $300).

Our findings in this study indicate correlations between biotypes and serotypes of haemophili, as well as between biotypes and clinical sources and age of patients from whom isolated. Our conclusions from this study are that more specific and definitive identifications of Haemophilus isolates than have heretofore been provided by clinical laboratories are important for overall patient-care as well as for endemiologic, nosocomial, epidemiologic, and taxanomic informational purposes.

A poster-session presentation of preliminary findings in this study was made at the 78th Annual Meeting of the American Society for Microbiology in Las Vegas, Nevada, 14-19 May 1978, and an abstact of the presentation was published in the abstracts of that meeting. A report based on this protocol is currently being prepared for submission for publication.

STATUS: (C)

TITLE: Rejuvenation of Outdated Human Erythrocytes and Evaluation of Frozen Blood Techniques

PRINCIPAL INVESTIGATOR: MAJ Robert T. Usry, MSC

WORK UNIT NO: 77/45

TECHNICAL OBJECTIVE

To determine the safety and efficacy of human red cells stored at $4^{o}C$ for 22-28 days that are biochemically modified (rejuvenated) prior to freeze-preservation; and to evaluate two techniques to freeze and deglycerolize human erythrocytes for utilization at Madigan Army Medical Center.

METHOD

Phase I: Rejuvenate and refreeze (as outlined in protocol) 30 units outdated O-positive or O-negative red cells and ship in dry ice to the Naval Blood Research Laboratory, Boston, MA, for complete freeze-thaw-wash recoveries on the red cells, bacterial cultures, and measurement of the red cell 2, 3-DPG, ATP, and potassium ion levels in addition to in vitro P_{50} levels. Red cell survival measurements will be performed on selected units.

Phase II: Rejuvenate and refreeze 30 units of expired blood, the same as Phase I with the exception of the removal of the supernatant solution containing glycerol, the solution used for biochemical modification, and plasma that is present in the concentrated red cells prior to freezing. These units will be shipped and evaluated as in Phase I.

Phase III: Same procedures as in Phase II with the exception that freezing will be accomplished in the original blood bag and shipped as in Phases I and II.

PROGRESS

(77 10 - 78 09) Restoration of ATP and 2, 3-DPG levels on 25 units of outdated blood stored in CPD preservative was accomplished utilizing Valeri's PIGP-A and PIGP-B solutions. These units were then frozen in the original blood bag (two bags per aluminum storage canister) and transferred to the Naval Blood Research Laboratory for evaluation of freeze thaw recoveries, bacterial cultures, 2, 3-DPG levels, ATP levels, and potassium determinations in addition to in vitro P_{50} levels. Results will be forthcoming.

STATUS: (O)

TITLE: Ambulatory Adolescent Health Care Needs: Implications for Pediatric Training Programs

PRINCIPAL INVESTIGATOR: MAJ Peter Johnsen, MC

WORK UNIT NO: 78/39

TECHNICAL OBJECTIVE

To determine from collated data of all Adolescent Clinic visits for one year (1) the common health care needs of this population of adolescents; (2) where the focus of teaching effort should be in training residents; (3) in which areas useful research could be entertained. This study will also serve a quality control function for the Adolescent Clinic.

METHOD

For one calendar year, assign each new patient a file card, including name, SSN, year of birth, sex, race, sponsor's rank, and status. For each patient visit, the physician will write the diagnoses of the problems encountered on that visit on the file card to be coded by the clinic staff. At the end of the year, the following data will be tabulated: (1) number of patients/patient visits; (2) number of patients/patient visits for each diagnostic category; and (3) demographic data: sex, year of birth, race, sponsor's rank and status. The collated data will then be evaluated for those areas in which resident education would be beneficial and a curriculum derived.

PROGRESS

(78 05 - 78 09) This project is ongoing with compilation of the data now in progress.

STATUS: (O)

TITLE: Early Detection of School Learning Problems During Kindergarten School Physicals Using Volunteer Staff and New Techniques

PRINCIPAL INVESTIGATOR: COL James H. Nelson, MC

WORK UNIT NO: 77/11

TECHNICAL OBJECTIVE

To determine if the newly devised PDQ (Denver Prescreening Questionnaire) is an accurate, rapid, and effective tool in the identification of the anticipated 10-15% of children entering kindergarten who will have school learning problems. Such information, necessary for comprehensive pediatric care, would be most valuable to physicians, school, and family before rather than after the problem becomes manifest.

METHOD

All children receiving a physical examination at Madigan on a mass scale basis for kindergarten will be given a PDQ (to be completed by parents) and a Goodenough Draw-A-Person (to be completed by child), supervised by pediatric clinic volunteer staff. Total number anticipated is 400. After analysis, this material will be added to the individual child's outpatient medical chart, as it is information helpful to future care of the child and has many of the same items to be found on the DDST's now added to the chart, and may be compared to growth charts. Normal PDQ's will have no follow-up, questionables will be phoned for repeat screening, and abnormals will have more thorough screening before referral to other resources, such as Child Guidance Clinic, or the actual classroom performance in school after five months will be determined.

PROGRESS

(77 10 - 78 09) This study is complete and a manuscript is in preparation for submission for publication. Although the PDQ is certainly not a screening tool or a developmental test, it does separate a group at high risk for demonstrating school achievement and readiness problems. The PDQ was well accepted by the children and their parents. Most parents welcomed this attempt to evaluate their child's school readiness in this cursory, yet effective, form.

STATUS: (C)

TITLE: The Role of Bacterial and Chlamydial Agents in Acute Epididymitis and the Effect of Antibiotic Therapy.

PRINCIPAL INVESTIGATOR: LTC John K. Podgore, MC

WORK UNIT NO: 78/20

TECHNICAL OBJECTIVE

To determine what role certain infectious agents (Mycoplasma, Neisseria gonorrhoeae, Chlamydia trachomatis, and aerobic coliform bacteria) play in the etiology and pathogenesis of acute epididymitis; and to compare two commonly used forms of therapy for treatment of epididymitis.

METHOD

Study population: All males seen with the diagnosis of acute epididymitis who are hospitalized at Madigan Army Medical Center and who have had no antibiotic therapy in the month preceding the current episode of epididymitis.

Controls: A group of age and race-matched controls will be selected from Ft Lewis military personnel undergoing routine physical examinations.

Two urethral swabs will be obtained using calcium alginate swabs; the first for culture of N. gonorrhoeae and Gram stain; the second for culture of C. trachomatis and U. urealyticum.

Urine specimens: The first 10 cc of voided urine and a midstream urine will be obtained. The sediment of the first voided urine and midstream urine will be examined for number of WBC per high-powered field and bacteria. Both urine specimens will be cultured quantitatively for coliforms.

Blood specimens: 10 cc will be obtained by venipuncture for serology for C. trachomatis.

Similar urine and blood specimens will be obtained from the controls.

When surgery is clinically indicated to rule out torsion of the testicle, direct cultures of epididymal fluid will be obtained at

scrotal exploratory surgery. Radionucleatide scrotal scans will be done on all patients within 48 hours to rule out testicular torsion.

Treatment: All patients will be placed at bed rest with scrotal elevation until afebrile and pain has subsided.

If no coliforms are seen on the initial unspun urine and the midstream urine culture shows less than 10^3 coliforms per ml, the patient will be randomly treated with 100 mg doxycycline b.i.d. for 10 days or with 500 mg ampicillin q.i.d. for 10 days. If the patient's medical records or history indicate possible allergy to either of these agents, the alternate safe agent will be administered.

If coliforms are seen on the initial unspun urine or grown from any specimen with colony counts greater than 10^3/ml, patients will be treated individually according to results of urine cultures and antibiotic sensitivity patterns. Patients will be instructed not to have intercourse for at least 14 days after initiation of treatment.

Follow-up: All patients will be reexamined at 3, 7, 14 days, and 6 weeks after initiation of therapy. The presence of scrotal erythema, edema, and tenderness will be noted and recorded by standard protocol. Repeat cultures will be performed at 7 and 14 days and 6 weeks for C. trachomatis, U. urealyticum, and any other pathogen initially recovered. Ten cc of convalsecent blood will be obtained for serologic testing at 14 days and 6 weeks.

PROGRESS

(78 04 - 78 09) Initial and follow-up procedures have been completed on 29 patients. The investigators hope to enroll at least 50 patients on this protocol. Data has been acquired on the initial patients, but no correlation will be done until the procedures have been completed on all subjects and controls.

STATUS: (O)

TITLE: A Survey of Chlamydia trachomatis Cervical Colonization in Late Pregnancy and Conjunctival and Naso-Pharyngeal Carriage in the First Six Months of Life

PRINCIPAL INVESTIGATOR: LTC John K. Podgore, MC

WORK UNIT NO: 78/41

TECHNICAL OBJECTIVE

To determine the baseline carriage rate of Chlamydia trachomatis in the endocervix during late pregnancy and its relationship to various factors including age, parity, socio-economic status, race, and the development of subsequent post-partum fever, neonatal conjunctivitis, and pneumonia.

METHOD

The study population will consist of pregnant military dependents seen at MAMC during the 35 week gestation examination and all infants of these women. Cervical specimens will be obtained on sterile cotton swabs during the 35 week pelvic examination, immediately placed into carrying medium and stored at -70°C, and transported to the isolation laboratory at the University of Washington weekly. Serum specimens will be obtained from a portion of blood routinely drawn at this time. Microimmunofluorescent serology for Chlamydia will be done according to standard methods. Conjunctival specimens and naso-pharyngeal specimens will be obtained at the nursery discharge examination and at 4 weeks, 2 months, and 6 months. Conjunctival specimens for Giemsa stain and bacterial and chlamydial cultures will be obtained from all study infants that present with acute conjunctivitis as will naso-pharyngeal specimens for Gram stain. Bacterial and chlamydial cultures will be obtained from all study infants that present with pneumonia during the first year of life. Serum will be obtained from all study infants at six months to measure serum antibody to Chlamydia by microimmunofluorescent methods.

PROGRESS

(78 07 - 78 09) This protocol is being done in conjunction with the protocol entitled "The Effect of Antibiotic Therapy in the Last Trimester of Pregnancy upon the Incidence of Neonatal Conjunctivitis and Pneumonia due to Chlamydia trachomatis" and will begin when that protocol receives approval from OTSG.

STATUS: (O)

TITLE: A Prospective Analysis of the Current Pediatric Screening Program (PSP) to Critically Evaluate Its Effectiveness and Application to Other Military Pediatric Clinics.

PRINCIPAL INVESTIGATOR: Carl E. Stracener, M.D., DAC, (COL, USA, Ret)

WORK UNIT NO: 77/44

TECHNICAL OBJECTIVE

To determine through a comprehensive data analysis the effectiveness of the PSP to identify and treat pediatric patients who prior to its conception had not been receiving comprehensive, organized health care past the first year of life. In addition, this project will detail the PSP organization, methodology, and availability of application to other military clinics using the paraprofessional services of local Red Cross volunteers.

METHOD

A prospective study of 100 routine screenings was conducted, including information concerning early detection of vision, speech and hearing deficiencies, deviant physical and psychomotor development, dental disease, high blood pressure, anemia, bacteriuria, significant family history and environmental influences, immunization lags, and potential learning disabilities. The statistics were analyzed to document the need and effectiveness of the PSP. An analysis of the follow-up treatment necessary for those individuals identified with abnormalities will be conducted. A detailed report will be submitted concerning the present PSP and the utilization of Red Cross volunteers to provide a reference source for other military hospitals interested in the establishment of such a program. In addition, the paper will relate the results of the prospective study and its significance in detecting the implementation of quality health care for pediatric patients. In conjunction with assisting other military hospitals in program implementation, a video tape of a representative family and medical history intake and routine screening appointment will be made using existing Madigan audio-visual facilities.

A Prospective Analysis of the Current Pediatric Screening Program to Critically Evaluate Its Effective and Application - Stracener

PROGRESS

(77 10 - 78 09) Due to the departure of the principal investigator, COL James H. Nelson, Carl E. Stracener, M.D., LTC, Ret., who is now employed at Madigan by the Department of the Army, has been appointed as the new principal investigator. Dr. Stracener was initially a professional assistant on this protocol.

The initial 500 cases have been completed, and a manuscript has been accepted for publication in the Western Journal of Medicine. This screening program, using well-trained volunteers, provided with adequate supervision and follow-up physical examination of the child, identified many new problems at minimal cost and proved an effective means of expanding quality health care.

Additional funds have been allocated to this project and another phase of the project has been started.

STATUS: (O)

TITLE: Maintenance of Patency of the Ductus Arteriosus in Congenital Cardiac Lesions. (Upjohn Cardiovascular Diseases Research Protocol #2907 - Multi-Clinic)

PRINCIPAL INVESTIGATOR: MAJ Warren H. Toews, MC

WORK UNIT NO: 78/44

TECHNICAL OBJECTIVE

This study will examine infants with cyanotic congenital heart diseases to see if the patency of the ductus can be maintained by infusion of Prostaglandin E_1. The minimal effective dose and side effects of this agent will be determined.

METHOD

This study is being done as a group study with Upjohn. In infants in whom blood is flowing through the ductus from the aorta to the pulmonary artery, a catheter will be placed through the umbilical artery to the first part of the descending aorta, at or just above its junction with the ductus. Prostaglandin E_1 will be infused continually into this region at the rate of 0.1 mcg/kg/min until the desired ductal effect is achieved, and then the dose will be decreased to 0.05 mcg/kg/min. In infants in whom blood flow is passing through the ductus from the pulmomary artery to the aorta, a catheter will be placed in the pulmomary artery proximal to the ductus arteriosus and Prostaglandin E_1 will be infused at the rate of 0.1 mcg/kg/min until the desired ductal effect is achieved, and then the dose will be decreased to 0.05 mcg/kg/min. Further dose adjustments in either case will be made, but doses greater than 0.1 mcg/kg/min will be documented as to the reason. In the event that the major artery cannot be catheterized, the infusion will be given into a large vein. The infusion will be continued until surgery can be performed - usually a matter of hours.. An angiogram will be performed before and after infusion as will serum creatinine, liver function studies, blood glucose, Ca, CBC, and urinalysis. Blood pressure, arterial blood gases, pH, temperature, pulse rate, respiratory rate, and general condition will be monitored hourly. Evidence of increased femoral pulses, decreased acidosis, increased urine output, or improvement of congestive heart failure will be noted. The investigator will monitor any changes in clinical condition and note an opinion as to its possible relationship to the drug.

Maintenance of Patency of the Ductus Arteriosus - Toews

ANALYSIS OF RESULTS: In decreased pulmonary blood flow, evidence of efficacy will be evaluated in the following ways: (1) increase in pO_2; (2) evidence of the patency of the ductus at surgery or at autopsy; (3) confirmation of ductal dilation with PGE_1 by angiograms. In interrupted aortic arch, evidence of efficacy will be evaluated in the following ways: (1) a decrease in the gradient in pressure between the pulmonary artery and the aorta; (2) increased femoral pulses; (3) decreased acidosis; (4) increased urine output; (5) improvement in congestive heart failure; (6) confirmation of ductal dilation with PGE_1 by angiograms.

PROGRESS

(78 09 - 78 09) This protocol is ongoing and will continue until complete FDA approval of the use of PGE_1 for maintenance of ductal patency is given. The technical part of the protocol has not been started as approval was received only two weeks before the end of the fiscal year.

STATUS: (O)

TITLE: Preventive Care Services for Infants: Evaluation of Problems and Outcomes

PRINCIPAL INVESTIGATOR: M. C. Yokan, M.D., DAC

WORK UNIT NO: 77/08

TECHNICAL OBJECTIVE

To evaluate both process and outcomes of preventive care services provided in a large clinic to infants from one month of age up to and including the one year checkup.

METHOD

Infants enrolled in the Well Child Clinic for the initial one month checkup and remaining in care at MAMC through the first year checkup, who are healthy single births, will have their records surveyed. We will assess time, personnel and funds required to provide customary preventive services to the normal infant population; level of completion of recommended available services, particularly routine immunization; complicance with instructions regarding safety measures, particularly provision of a safe restraint device for the infant in the family automobile; and frequency of consultations to other departments and of visits to other clinics for care of illness. Also assessed will be incidence of accidents or other preventable type of illness; incidence of significant problems detected; overall maintenance of good health; relation of demographic characteristics to health problems. A survey will be made of other military pediatric facilities by mail for purposes of comparison of the scope of preventive care services provided.

PROGRESS

(77 10 - 78 09) This project has been completed. Preventive services have proven valuable and the benefits of increased emphasis on creating a safe environment are now obvious.

A manuscript entitled "Infant Preventive Care in a Young and Healthy Population" by Yokan, C., Turner, C., Knudson, R.P., Stracener, C., and Alden, E.R., has been accepted for publication in Military Medicine.

Preventive Care Services for Infants - Yokan

Publication: Yoakn, C. and D'Onofrio, C.: Application of Health Education Methods to Achieve Higher Immunization Rates. Public Health Reports 93:211-215, 1978.

STATUS: (C)

TITLE: A Clinical Validation Study of the Walter Reed Neuropsychological Screening Battery

PRINCIPAL INVESTIGATOR: CPT Raymond A. Parker, MSC

WORK UNIT NO: 75/35

TECHNICAL OBJECTIVE

To determine empirically the clinical usefulness of the Walter Reed Neuropsychological Screening Battery, a multi-test battery designed to permit certain inferences concerning the organic integrity of an individual's cerebral cortex.

METHOD

Patients will be referred to Neuropsychology from Neurology with (1) clear-cut unequivocal evidence of cortical lesions with an established neurological diagnosis and (2) with no CNS pathology that can be demonstrated (control group). After establishing a final diagnosis on a patient, Neurology will fill out a validation study data sheet and hold the data sheet for the final analysis. Neurology will then contact Neuropsychology and arrange for the patient to be assessed with the Walter Reed Nueropsychological Screening Battery. After approximately ten patients have been evaluated for each of the two groups, the data sheets will be obtained from Neurology, and a comparison of the impressions from Neuropsychology and Neurology will be made. The neurological impression will be the validation criterion for each patient. Contingency tables such as illustrated in the protocol will be used to illustrate the results for each of the two neuropsychologists and Neurology. An appropriate Chi-square statistic will be used to evaluate the statistical significance of the agreement between Neuropsychology and Neurology. The results will be interpreted and discussed appropriately.

PROGRESS

(77 10 - 78 08) This project was terminated due to lack of tests and procedures that can be administered in a short enough time to give meaningful results.

STATUS: (T)

TITLE: The Fort Lewis Smoking Control Clinic: A Major Follow-Up Study

PRINCIPAL INVESTIGATOR: CPT Raymond A. Parker, MSC

WORK UNIT NO: 78/01

TECHNICAL OBJECTIVE

To determine the effectiveness of the treatment procedures in the Fort Lewis Smoking Control Clinic on a large number of clients (172) over a significant time period (six months). Abstinence rates, percent of base-line smoking rates, and actual changes in cigarettes smoked per client per day will be examined. Additionally, the relationship of certain easily attainable demographic variables (age, sex, length of time as a smoker) to outcome of smoking treatment will be examined.

METHOD

Smoking treatment and outcome data on 172 clients were gathered from the Fort Lewis Smoking Control Clinic files and statistically analyzed.

PROGRESS

(77 10 - 78 05) The data have been gathered and analyzed. A report on this study has been accepted for publication in Professional Psychology.

STATUS: (C)

TITLE: Electrocardiographic Effects of Two Tricyclic Antidepressants in Depressed Patients

PRINCIPAL INVESTIGATOR: Allan H. Pribble, M.D.

WORK UNIT NO: 77/91

TECHNICAL OBJECTIVE

To compare the electrocardiographic changes in patients given equal milligram doses of amitriptyline and desipramine and to associate observed changes with individual plasma levels of the drugs.

METHOD

This study will be done in conjunction with the Outpatient Psychiatry Clinic, American Lake VA Hospital, Tacoma, WA. Forty depressed adult outpatients will be studied in a double-blind, cross-over trial. Only patients with a Zung SDS index of 55 or more and who meet the modified Feighner criteria for depression will be admitted to the study. After informed consent has been obtained, a medical history will be taken and an ECG will be performed. A physical examination will be given and laboratory tests will be done, including a blood chemistry profile, CBC, and plasma tricyclic antidepressant level--totalling about 25 cc. Patients will be randomly assigned to either the DMI-AMT or AMT-DMI sequence. Patients will be evaluated weekly for changes in electrocardiograms and to determine the plasma antidepressant concentration. A weekly Zung SDS will be obtained to monitor the clinical progress of the patient. At the conclusion of the study, a blood sample will be taken for a final blood chemistry and plasma tricyclic level. Patients considered in need of further antidepressant therapy will be referred to the Psychiatric Service for continued treatment.

PROGRESS

(78 03 - 78 09) Because of administrative and recruiting difficulties, this project was terminated after completion of approximately 15-20 subjects. Despite being far short of the goal of 40 subjects, an abstract is being prepared and will be submitted to an appropriate meeting.

STATUS: (T)

TITLE: An Investigation to Compare the Effect of Renal Function of Conservative versus Surgical Management of Blunt Renal Trauma in Canines

PRINCIPAL INVESTIGATOR: CPT Carl F. Cricco, MC

WORK UNIT NO: 76/16

TECHNICAL OBJECTIVE

To compare the morbidity and mortality of conservative (non-operative) versus surgical treatment of cortical lacerations analagous to those produced by non-penetrating trauma in man; to compare pre- and post-trauma renal function in these two groups and determine the therapy that provides the maximum preservation of renal function; and to determine the effect of these two therapeutic modalities on the development of hypertension via the renin-angiotensin system.

METHOD

Ten dogs weighing 25-35 pounds will be used for long term management. These dogs will be divided into two groups (surgical and conservative). Baseline CSC, Na, BUN, creatinines will be drawn. After the induction of anesthesia, pre-trauma urograms will be obtained in addition to urinalysis, urine culture and blood pressure. Only one renal unit will be studied so that each dog can act as his own control. Trauma will be induced through a flank incision by driving a dull cold chisel one cm into the lower pole cortex to form a cross-shaped laceration. The kidneys will be replaced and a 30-minute post-trauma arteriogram will be obtained. The dogs to be treated surgically will undergo heminephrectomy and the remainder will be observed. Three months post-trauma, repeat laboratory studies to include renins, BP, urograms, and arteriograms will be taken. The animals will then be sacrificed and the kidneys examined both grossly and microscopically.

PROGRESS

(77 10 - 78 09) The initial protocol has been completed. The results look very promising. Consultation with statistician reveals that larger numbers of data must be obtained. Therefore, the project is to be continued to allow a minimum of 12 more dogs to be done. MAJ Jonathan Vordermark, MC, completed the initial phase of the protocol. CPT Carl F. Cricco, MC, has been appointed as principal investigator to complete the additional phase.

STATUS: (O)

TITLE: Brainstem Electric Response Audiometry with High Frequency Hearing Loss

PRINCIPAL INVESTIGATOR: CPT Jeffrey W. Davies, MSC

WORK UNIT NO: 77/87

TECHNICAL OBJECTIVE

To develop norms for usage of a new procedure "VIII nerve tumor detection with brainstem electric response audiometry" in patients with high frequency hearing loss.

METHOD

The investigators will determine the latencies of response on 100 adult patients with differing degrees of known cochlear hearing loss to establish "cochlear norms." They will then statistically analyze the latency with the severity of cochlear hearing loss to determine how much severity of cochlear hearing loss affects latency. Norms will then be established so that other diagnosticians can use them as a correction factor to rule out an acoustic neuroma in patients with high frequency hearing loss.

PROGRESS

(77 10 - 78 09) This study has been completed and a manuscript is in preparation for submission of results for publication. Due to the departure of CPT S. Dean Harmer, MSC, the original principal investigator, CPT Davies was appointed principal investigator.

STATUS: (C)

TITLE: An Evaluation of the Safety and Efficacy of Cyanoacrylate Ester in Ossicular Reconstruction and Nerve Graft Anastomosis in the Guinea Pig Middle Ear

PRINCIPAL INVESTIGATOR: COL William H. Gernon, MC

WORK UNIT NO: 77/88

TECHNICAL OBJECTIVE

To determine the safety and efficacy of cyanoacrylate ester in the middle ear; specifically, for ossicular reconstruction for histological changes in the oval window area and in the facial nerve. In addition, the use of this compound in tympanoplasty would be a natural extension of this project. The intended purpose of this study is to open the door for the use of cyanoacrylate ester in human surgery, initially on an experimental basis.

METHOD

The surgical anatomy of the guinea pig ear is well known with two good approaches. The investigators propose to use Histoacryl and Crazy Glue to do interpositions (incus) on a test group of guinea pigs as well as place glue on the facial nerve, perhaps to do facial nerve anastomoses, and to place the glue in the oval window area. Approximately 39 animals would be utilized. At 3, 6, and 12 months, 12 experimental animals and one control animal would be sacrificed. Histological temporal bone studies would then be conducted at AFIP.

PROGRESS

(77 10 - 78 09) The middle ears of 16 animals were opened and the ossicles fixed to the attic with tissue glue. When the animal's ear was involved with otitis media, this was not possible. In the sixteen animals, the facial nerve was exposed and transected and then reapproximated with tissue glue.

An Evaluation of the Safety and Efficacy of Cyanoacrylate Ester - Gernon

Plans to sacrifice a certain number of animals at 3, 6, and 12 months have not been carried out as there was a problem with anesthesia and infection post-operatively, and to date only four animals are surviving.

A curtailment in funds has restricted our supplies and material for use in this surgical procedure, making it very difficult to do more animals. Most of the equipment and expendable supplies have to be brought from the hospital, which is time consuming and inefficient. When the budget problem improves, plans to do more animals will be scheduled.

Temporal bone processing has been scheduled at the AFIP by the ENT section by CPT Hymes, USN, and he is looking forward to helping us on this project.

STATUS: (O)

TITLE: Parent-Infant Screening Program

PRINCIPAL INVESTIGATOR: CPT S. Dean Harmer, MSC

WORK UNIT NO: 77/80

TECHNICAL OBJECTIVE

To accurately identify those newborns suspected of having significant hearing loss since much can be done to help the hearing imparied child if the loss is detected early in life.

METHOD

A questionnaire concerning response to sound will be given to the mother of each newborn child when she takes the child home for the first time. The mother will return the questionnaire to the baby's first checkup. It will be reviewed by the examining physician who will note the results in the baby's record. Abnormal findings will be referred to Audiology Clinic for audiometric testing, and the questionnaire will be returned to the Audiology Clinic for a compilation of results.

PROGRESS

(77 10 - 78 05) This protocol has been terminated due to lack of response from questionnaires resulting in an inadequate data base for meaningful scientific analysis and due to the departure of the principal investigator.

STATUS: (T)

TITLE: Medical Treatment of the Frey Syndrome

PRINCIPAL INVESTIGATOR: COL Leonard L. Hays, MC

WORK UNIT NO: 76/06

TECHNICAL OBJECTIVE

1. To study objectively the true incidence of the Frey Syndrome in post-parotidectomy patients by means of the Minor Starch Iodine Test.

2. To determine the effect of, and patient satisfaction with, medical management comparing on a double blind basis topical use of a placebo, varying concentrations of scopolamine hydrobromide, and the newer anticholinergic agent, glycopyrrolate.

3. To investigate the value and practicality of iontophoresis of the above agents to increase the duration of satisfactory control of sweating.

4. To compare the topical use of a patient's most effective antiperspirant on the involved facial skin with the result from the topical use of the most effective agent in the double blind series for that patient.

METHOD

Phase I - Double-blind treatment with ½%, 1%, and 3% scopolamine hydrobromide cream, 0.1% glycopyrrolate, and a placebo; comparison by the patient as to effectiveness; and retreatment after drug dosage adjustment if the patient fails to respond.

Phase II - Utilize iontophoretic introduction of the best anticholinergic agent to a group of volunteers with significant sweating symptoms and to a group who are medical failures and compare action and duration of action with iontophoretic introduction using tap water, Ringer's lactate, or saline.

Phase III - Patients who failed medical treatment or have become dissatisfied with the medical treatment and have significant symptoms confirmed on minor startch-iodine testing will be offered surgery such as flap elevation or tympanic neurectomy.

Medical Treatment of the Frey Syndrome - Hays

PROGRESS

(77 10 - 78 09) Phases I and II of this protocol have been completed and an article giving the results has been accepted for publication in Laryngoscope.

At present, ten of the original patients are being studied in a double blind format comparing glycopyrrolate in an improved cream base to a roll-on dispenser application. Also, the drug's clinical stability from date of manufacture and patient tolerance to the medication over long term intermittent use will be studied.

STATUS: (O)

TITLE: Teaching Program for Practical Microsurgery

PRINCIPAL INVESTIGATOR: MAJ Robert Kenevan, MC

WORK UNIT NO: 77/92

TECHNICAL OBJECTIVE

To establish a formal training program at Madigan Army Medical Center in clinical microsurgery.

METHOD

The teaching program will be established at Clinical Investigation Service, and a room will be set aside for the project where equipment for the microsurgery can be housed. A schedule of two afternoons per week will be set aside for teaching sessions. Animal model preparations (cadaver and live) will be developed by the veterinary surgical consultant with the support of the clinical teaching staff. Sessions will begin with lectures, followed by practical exercises in anatomy and step-by-step instruction in the surgical techniques.

PROGRESS

(77 10 - 78 09) Instruments have been obtained and an operating microscope has been periodically loaned to the laboratory from Otolaryngology. The techniques of microvascular surgery have been utilized in laboratory situations. More practice is necessary to refine the techniques and to develop clinical models for orderly instruction in the fundamentals of microsurgery techniques.

MAJ Robert Kenevan, MC, has been assigned as principal investigator to replace MAJ Stanley Jackson who has been reassigned to another hospital.

STATUS: (O)

TITLE: Jejuno-ileal Bypass Surgery for Morbid Obesity

PRINCIPAL INVESTIGATOR: COL Joseph C. McDonald, MC

WORK UNIT NO: 77/81

TECHNICAL OBJECTIVE

To reduce the morbidity and mortality of morbidly obese patients by achieving weight reduction through partial defunctionalizing of the small bowel. This protocol was activated per a message from HQDA, DASG-HCP, 180800Z, Mar 77.

METHOD

Subjects must demonstrate a minimum of 100% above ideal body weight; a weight problem for five years; evidence of failure of dietary and/or group therapy measures for weight reduction; age under 50 years; absence of causative endocrine or metabolic dysfunction or unrelated medical disease which would contra-indicate operation; presence of complications of obesity; no history of ethanol abuse and a commitment to avoid ETOH for three years postoperatively; mental and emotional stability to tolerate the operation and its postoperative sequelae; and assurance of cooperation in the conduct of necessary pre- and post-operative studies. Once selected for jejuno-ileal bypass, the patient will undergo extensive pre-operative evaluation by the Gastroenterology Service, followed by jejuno-ileal bypass and ileo-cecostomy. Immediate post-operative care will be carried out by the surgeons with appropriate consultation. Long term follow-up care will be conducted by each involved service.

PROGRESS

(77 10 - 78 09) Two new patients have been operated upon since the Annual Report of FY 77. The first did not lose any weight, apparently because she increased her dietary intake. She has not had any other complication. The second patient was done without complication. She is now being treated at another medical center and losing weight appropriately.

STATUS: (O)

TITLE: Evaluation of One Stage Longitudinally Reduced Ileal Ureters with the Use of the Auto Suture in Dogs

PRINCIPAL INVESTIGATOR: LTC Robert Modarelli

WORK UNIT NO: 77/69

TECHNICAL OBJECTIVE

To determine the chemical aberrations that occur in the urine and serum between an ileal ureter and its contralateral in situ ureter; to compare quantitatively the changes that occur in the urine of longitudinally reduced ileal ureters and its contralateral in situ ureter; to observe radiographically the function of ileal ureters and longitudinally reduced ileal ureters; to evaluate the applicability of the Auto Suture, Models TA-55 and GIA, in intestinal urinary conduit and urinary bladder surgery; and to study the long-term effects of variably longitudinally reduced ileal ureters on renal function and on qualitative and quantitative changes in urine and serum.

METHOD

Phase I - divide the urinary bladder in a female dog with the GIA Auto Suture; obtain baseline split renal collections for volume, electrolytes, BUN, creatinine, Ca, phosphorus, protein, glucose, oxalate, pH, and osmolality determinations; obtain simultaneous serum samples for electrolyte, BUN, creatinine, Ca, phosphorus, glucose, and protein determinations; and determine the renal function by excretory urogram.

Phase II - Group I - one ureter will be replaced with a pedicled vascularized distal ileal segment according to techniques used by Goldstein and others. Group II - will have an appropriate segment of ileum isolated on a vascular pedicle. An ileo-ileostomy is carried out to reestablish bowel continuity. The pedicled ileal segment is sutured longitudinally parallel to the mesenteric border of the ileum by applying the TA-55 or GIA Auto Suture, longitudinally bisecting the ileum between its mesenteric and antimesenteric borders. The sequence is repeated until the ileal segment is longitudinally bisected and a 50% reduction in surface area is noted. A proximal ileo-pyelo and a distal ileo-vesicle anastomosis is carried out. Group III - will

undergo the same procedure as Group II dogs except that the ileal segment will be reduced to an even smaller lumen, i.e., a 24 French caliber ileal tubular segment.

Qualitative and quantitative split urine collections and serum determinations are repeated as in Phase I in the postoperative period. Radiologic contrast studies, consisting of intravenous pyelograms, retrograde cystograms and fluoroscopic evaluation of the upper and lower urinary tracts, will be done. Urine collections, serum determinations, and radiologic contrast studies will be repeated at 6 weeks, 3, 6, and 12 months post-ureteral replacement surgery. Following initial evaluation of what appears to be the more ideal ileal segment for ureteral replacement, a contralateral nephrectomy will be considered in order to simulate more effectively the patient who has only one functioning kidney remaining. At completion of the investigation, unilateral nephrectomies with hemicystectomies will be performed or the dogs will be sacrificed for gross and microscopic evaluation of kidneys, ileal ureters, and bladder.

PROGRESS

(77 10 - 78 09) Two dogs remain on this study. One has a longitudinally reduced ileal ureter and the other has a total ileal replacement. Two other dogs have died due to leaking of the anastomoses. The present plan is to do IVP's within the next month on the two remaining dogs and to decide at that time whether to sacrifice them and study their anastomotic sites. If meaningful data is obtained, a report will be written for possible publication.

STATUS: (O)

TITLE: Lid Magnets for Correction of Orbicularis Palsy

PRINCIPAL INVESTIGATOR: COL Stanley C. Sollie, MC

WORK UNIT NO: 75/27

TECHNICAL OBJECTIVE

To study the effects of the insertion of lid magnets on the tarsal plates of the lids involved in seventh nerve palsy.

METHOD

Patients with seventh nerve palsy will be evaluated, and, if the palsy persists longer than six months without showing improvement and if the eye is affected by the lack of lid closures, these patients will be considered for the surgery. The surgery consists of implanting lid magnets, supplied through Wolfgang D. Muhlbauer, Department of Plastic and Reconstructive Surgery, Klinikum rechts der Isar of the Technical University, Munich, Germany. A skin incision is made in the upper and lower lid and the magnets are sutured to the tarsus. The skin incision is then closed.

PROGRESS

(77 10 - 78 09) During FY 78, two new patients were operated with good results, and both are still successful. Three reoperations were performed. Two were successful with good results; the third had infection and removal of the magnets was necessary.

STATUS: (O)

TITLE: The Incidence of Paraspinal Musculature EMG Abnormalities in Cancer Patients with Known Spinal Metastasis

PRINCIPAL INVESTIGATOR: LTC Surinderjit Singh, MC

WORK UNIT NO: 77/37

TECHNICAL OBJECTIVE

To systematically evaluate paraspinal skeletal musculature in cancer patients with bone scan evidence of spinous metastasis by electromyographic techniques to determine the incidence of abnormal findings and to see if a specific pattern of abnormality exists which might be useful as a diagnostic screening technique.

METHOD

Patients who have specific cancer types that frequently metastasize to bone, such as breast carcinoma, prostatic carcinoma, lung carcinoma and/or multiple myeloma, will be eligible for this study. Only those patients who have documented scan evidence of metastasis will be included in the initial study. EMG will be performed on the back musculature, looking for abnormalities. If abnormalities are noted, then the skeletal musculature of the legs will be examined using the same technique. The number and percentage of electromyogram abnormalities will be analyzed as to distribution, and the data will be evaluated to see if a particular EMG abnormal pattern is present. Statistical analysis employing the Chi square method will be utilized between the various diagnostic cancer groups. Significance will be determined to the 5% level.

PROGRESS

(77 10 - 78 09) This protocol has been terminated due to a lack of patients and insufficient clinical material.

STATUS: (T)

TITLE: Child Abuse, Job Satisfaction, and Social Isolation Among Military Families

PRINCIPAL INVESTIGATOR: MAJ Larry R. Sanderlin, MSC

WORK UNIT NO: 78/06

TECHNICAL OBJECTIVE

A MAMC study found the child abuse rate to be disproportionately higher among garrison/support troops than among combat infantry soldiers or other soldiers whose jobs require a considerable amount of skill and/or a significant amount of technical training. William Beaumont Army Medical Center had similar findings. It is therefore hypothesized that in the military there will be an inverse relationship between child abuse and job satisfaction. It is also hypothesized that there will be a positive correlation between social isolation and child abuse among military families. This study will test these hypotheses.

METHOD

The study will include three groups with 100 soldiers each.

Group A will come from patients referred to MAMC Social Work Service as the result of child abuse and/or neglect.

Group B will be a matching sample referred for other psychosocial problems, but who are not child abusers.

Group C will be a stratified random sample who have not been identified as having any type of psychosocial problem.

All participants will be asked to complete a Job Description Index and Srole's Anomie Scale (to measure social isolation). After the data collection is completed, the results will be analyzed at the University of Washington Academic Computer Center.

PROGRESS

(77 12 - 78 09) Due to the departure of the principal investigator, MAJ Larry R. Sanderlin, MSC, has been designated as the principal investigator. Approximately one-third of the data has been collected with no major problems encountered. The project should be completed approximately second quarter of FY 79.

STATUS: (O)

TITLE: The Effects of Low Exposure Levels to Anesthetic Gases in Operating Rooms at MAMC

PRINCIPAL INVESTIGATOR: CPT Robert R. Byland, MSC

WORK UNIT NO: 77/72

TECHNICAL OBJECTIVE

To evaluate the levels of anesthetic gas the anesthesiologist and operating room personnel receive with the present type of gas delivery, recovery, and disposal systems used at this center.

METHOD

1. Coordinate with OR supervisor and anesthetist as to the length of time various operations take and the gases used.
2. Schedule twelve operations to test for gases.
3. Use previous ventilation survey results for room volume and air turnover rate to predict gas concentrations.
4. Determine prior to any operation the effect of opening and closing of OR doors has on the air flow.
5. Set up the Miran I.R. unit and calibrate.
6. Using the 10-foot sampling hose, collect samples during the operation.
7. Samples will be collected around gas delivery systems, the anesthesiologist, and OR personnel's breathing zones.
8. Samples will be collected every 15 minutes and recorded on a strip chart.
9. Analysis of collected data.

PROGRESS

(77 10 - 78 10) Equipment and materials are in house and data collection is to start within a few weeks.

STATUS: (O)

TITLE: An Analysis of the Prevalence, Severity, and Correlates of Drug and Alcohol Abuse at a Large Army Installation

PRINCIPAL INVESTIGATOR: John P. Allen, PhD, DAC

WORK UNIT NO: 78/21

TECHNICAL OBJECTIVE

To provide answers as to the availability of illicit drugs (both on post and in the civilian community); the incidence and nature of illicit durg and alcohol abuse at Fort Lewis and Madigan Army Medical Center; the relationship of substance abuse to social climate, authority relationships, and military preparedness; the relationship to rank, demographic characteristics, abuse-non-abuse characteristics of individuals, etc.; the relationship of alcohol abuse and drug abuse; what characteristics observable by commanders and supervisors define high risk individuals; the psychological/demographic correlates of alcohol-related offenses; the effectiveness of urinalysis as a deterrent; to what groups the ADAPCP can most effectively address its educational/preventive aspects; and what concrete, feasible and promising suggestions can be made to reduce local and Army-wide problems with drug and alcohol abuse.

METHOD

Sample population will be randomly selected across military ranks on the basis of SSN's and will consist of approximately 3,000 soldiers. After appropriate training, the survey will be administered by battalion adjutants. Data will be submitted to a braod range of correlational and multivariate analyses and will attempt to provide information as stated in the objective section above. Considerable effort will be expended both in data interpretation and in exploration of the preventive health care implications of these statistical analyses. After interpretation of statistical analyses and formulation of action suggestions, the results and proposed course of action will be submitted to Headquarters, 9th Infantry Division and Madigan Army Medical Center (and, if appropriate, to OTSG, HSC, and other higher headquarters). Appropriate information will be disseminated to major subordinate commanders and Alcohol and Drug Dependency Intervention Council.

An Analysis of the Prevalence, Severity, and Correlates of Drug and Alcohol Abuse at a Large Army Installation - Allen

PROGRESS

(78 02 - 78 09) All data has been collected and transferred to Hollerith cards. The cross-classification of content items by rank (E1-E4 and E5-E9) by battalion is currently being calculated. The post-wide tally of each content item by each specific rank within the enlisted, warrant officer, and commissioned officer samples is also being run.

Future analyses will deal with four broad areas: (1) Deterrents to seeking treatment; (2) The relationship between morale and substance abuse; (3) High risk predictors of substance abuse; (4) Respondents' preceptions of the severity of the substance abuse problem and the Army's attempts to treat it.

STATUS: (O)

TITLE: SWOG 7410, Chronic Lymphocytic Leukemia Protocol Utilizing Cyclophosphamide, Adriamycin, and Prednisone.

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/13

TECHNICAL OBJECTIVE

1. To determine the response rate, both complete and partial, in chronic lymphocytic leukemia, to combination chemotherapy with:

   A. Cyclophosphamide, adriamycin, and prednisone (CAP) as primary therapy in patients who have had no prior chemotherapy.

   B. CAP as secondary therapy for those patients who have previously received low dose chlorambucil.

2. To assess the effectiveness of intermittent cyclophosphamide and prednisone in maintaining a remission.

METHOD

After meeting stringent criteria, all untreated patients with CLL or patients previously treated with a low dose of chlorambucil only, at least four weeks prior to start of therapy, will be entered in the study.

Remission Induction: cyclophosphamide - 500 mg/M^2, I.V., on day 1
adriamycin - 50 mg/M^2, I.V., on day 1
prednisone - 100 mg/day, p.o., for 5 days

After eight courses of induction therapy (or those having attained remission between three & eight courses), those patients who have attained complete or partial remission will receive maintenance therapy consisting of:

cyclophosphamide - 750 mg/M^2, I.V., on day 1
prednisone - 100 mg/day, p.o., for 5 days

Course will be repeated every three weeks until relapse in cases in complete remission or increasing disease is evident in cases in partial remission.

PROGRESS

(77 10 - 78 09) No patients were entered on the study in FY 78.

STATUS: (O)

TITLE: SWOG 7434, 5-FU+Mitomycin C vs 5-FU+MeCCNU in GI Malignancies

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/16

TECHNICAL OBJECTIVE

1. To determine and compare the effectiveness of two combination chemotherapies in gastrointestinal carcinomas: 5-Fluorouracil infusion and Mitomycin C vs 5-Fluorouracil infusion and Methyl CCNU.

2. To compare the toxicities produced by these two combinations to allow the decision as to which of the two regimens is superior.

3. To compare the results of this study with the results observed in the SWOG 7302 protocol, which was 5-FU bolus vs 5-FU bolus + Methyl CCNU.

METHOD

After randomization, patients will receive one of the above drug combinations. Initial treatment, subsequent dosage adjustment, dose levels, and treatment schema are as outlined in the protocol.

PROGRESS

(77 10 - 78 09) No patients have been entered on this protocol, and it has been terminated.

STATUS: (T)

TITLE: SWOG 7440, Adjuvant Chemotherapy for Osteogenic Sarcoma

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/17

TECHNICAL OBJECTIVE

1. To determine the efficacy of combination chemotherapy with CY-VA-DIC (cyclophosphamide, vincristine, adriamycin, and DIC) in preventing the development of metastases in patients with osteogenic sarcoma who have received definitive surgery for their primary lesions and who have no evidence of residual disease.

2. To determine the survival and disease-free interval pattern of patients on this study to be compared to historic controls in the medical literature.

METHOD

Patients with a confirmed diagnosis of osteogenic sarcoma who have received definitive surgical therapy and have no evidence of metastases following surgery and who have not received any prior therapy (other than surgery) shall be treated with a chemotherapy regimen consisting of vincristine, adriamycin, cyclophosphamide, and DIC as outlined in paragraph 5.0 of the protocol.

PROGRESS

(77 10 - 78 09) No patients have been entered on this protocol.

STATUS: (O)

TITLE: SWOG 7510, Intensive Adjuvant Chemotherapy with or without Oral BCG Immunotherapy for Patients with Locally Advanced Adenocarcinoma of the Large Bowel

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/18

TECHNICAL OBJECTIVE

To determine the efficacy of adjuvant chemotherapy with the highly effective combination of Methyl CCNU (MeCCNU) and 5-Fluorouracil (5-FU) and to determine whether this is added to by immunotherapy with oral Bacillus Calmette-Guerin (BCG) on the disease-free interval and survival of patients with Duke C large bowel adenocarcinoma.

METHOD

Patients will be randomly assigned to either of the two following regimens:

Chemotherapy alone - Methyl CCNU, given orally on day 1, plus intravenous 5-Fluorouracil, given intravenously weekly for three doses would constitute one course. Courses would begin every eight weeks.

Chemotherapy plus immunotherapy - Chemotherapy as described above plus immunotherapy in the form of oral BCG given every two weeks.

PROGRESS

(77 10 - 78 09) Seven patients are currently entered on this study. Five patients have finished chemotherapy (12 mo) and are free of disease at 14, 15, 17, 21, and 21 months, respectively, after treatment start. Two patients are still on treatment (4 and 11 mo) without evidence of clinical disease.

STATUS: (O)

TITLE: SWOG 7610, Chemotherapy of Disseminated Testicular Cancer with Vinblastine, Bleomycin, Cis-Diammine-dichloroplatinum, Chlorambucil, and Actinomycin-D

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/19

TECHNICAL OBJECTIVE

1. To determine the effectiveness of the drug combination, vinblastine, bleomycin, and Cis-diamminedichloroplatinum (II) (CACP) in the remission induction of disseminated testicular carcinoma.

2. To determine the duration of remission with a maintenance drug combination of chlorambucil and actinomycin-D, alternating with vinblastine.

METHOD

All patients meeting criteria as outlined in the protocol are to receive vinblastine, bleomycin, and CACP for two months. At that point, patients judged to be in complete remission, partial remission, or stable will receive an additional two months of therapy All partial and complete responders at four months will then enter the remission maintenance program. Patients with increasing disease at two months, or stable or increasing disease at four months are to be taken off study.

PROGRESS

(77 10 - 78 09) No patients have been entered on this study.

STATUS: (O)

TITLE: SWOG 7432, Vincristine, BCNU, Adriamycin, and Prednisone (VBAP) in Previously Treated Myeloma Patients

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/23

TECHNICAL OBJECTIVE

To evaluate the frequency and degree of response with Vincristine-BCNU-Prednisone-Adriamycin combination (VBAP) in patients who failed to respond on alkylating agents with or without Prednisone.

METHOD

VBAP will be administered as outlined in the protocol. The minimum duration of the initial induction treatment is 4 months; the maximum duration 9 months. If remission is confirmed, the patient will continue treatment to disappearance of "M" peak or exacerbation of disease. If no response is confirmed after 9 months or if there is progression of disease at 4 months, the study should be terminated.

PROGRESS

(77 10 - 78 02) Two patients were entered on this protocol.

1. Multiple myeloma - patient died with progressive disease after receiving only one dose.

2. Recurrent lymphoma - on treatment for six months with partial response. Patient subsequently left the area and discontinued this treatment.

This protocol has been terminated and replaced by SWOG 7719.

STATUS: (T)

TITLE: SWOG 7436, Combined Modality Therapy of Breast Carcinoma

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/24

TECHNICAL OBJECTIVE

To compare the effect of two adjuvant chemotherapy programs upon the time to recurrence and upon the percentage of recurrences in post-operative breast carcinoma patients who have a high risk of developing metastases. To compare the effect of these adjuvant chemotherapy programs upon the survival pattern of such patients.

METHOD

Melphalan and combination (5-Fluorouracil, Methotrexate, Vincristine, Cyclophosphamide, Prednisone) will be used as chemotherapy as outlined in the protocol. The adjuvant chemotherapy will be instituted (regardless of radiation therapy) two weeks after radical mastectomy, unless local or systemic post-operative complications of surgery contraindicate onset of therapy. In such cases, therapy will be instituted when the primary physician involved feels it is not contraindicated by the clinical condition of the patient. The interval between surgery and the institution of adjuvant chemotherapy cannot be greater than six weeks for entry into the study. All therapy will be discontinued after one year.

PROGRESS

(77 10 - 78 09) Four patients are entered on this study. All with complete response (no recurrence) after 0, 3, 4, and 5 months of treatment.

STATUS: (O)

TITLE: SWOG 7509, 5-FU, MeCCNU + Radiotherapy With or Without Testolactone for Localized Adenocarcinoma of the Exocrine Pancreas

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/25

TECHNICAL OBJECTIVE

To evaluate the effect on survival of intensive radiotherapy and chemotherapy (5-FU and MeCCNU) of localized pancreatic adenocarcinoma. To evaluate, in a randomized manner, any beneficial effect of testolactone when added to the above regimen.

METHOD

Patients will be stratified according to the type of surgery performed: biopsy only, palliative bypass procedure, or resection. They will then be randomized to receive either testolactone, 5-FU, MeCCNU, and radiation therapy, or 5-FU, MeCCNU, and radiation therapy without testolactone. Patients surviving for one year will be offered a second-look operative procedure at the discretion of the attending physician for the purpose of restaging, resecting or palliating appropriately. Patients without evidence of disease at this second-look procedure will continue chemotherapy for one more year only. Those who are found to have tumor will also receive chemotherapy for one year but, at the end of this period, another re-exploration will be offered and patients found to be free of disease will be given an additional year of chemotherapy. Patients with persistent tumor at this time (third operation) will continue on chemotherapy indefinitely.

PROGRESS

(77 10 - 78 09) No patients have been entered on this protocol, and it has been terminated.

STATUS: (T)

TITLE: SWOG 7517, Therapy of Squamous Cell Carcinoma of the Head and Neck Using Combination Bleomycin, Vincristine, and Methotrexate

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/26

TECHNICAL OBJECTIVE

To determine the toxicity and effectiveness of various dosage levels of a combination of bleomycin, oncovin, and methotrexate in the treatment of patients with squamous cell carcinoma of the head and neck.

METHOD

A total of thirty patients with squamous cell carcinoma of the head and neck will be treated with a combination of bleomycin, vincristine, and methotrexate as outlined in the protocol. Patients must receive two complete cycles of therapy to be evaluable for response. The duration of response shall be measured from the time that a partial response is achieved to the time at which progression is apparent.

PROGRESS

(77 10 - 78 09) No patients have been registered on this protocol.

STATUS: (O)

TITLE: SWOG 7519, Phase III Study of Squamous Cell Carcinoma of the Head and Neck Region

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/27

TECHNICAL OBJECTIVE

To determine whether a three-drug combination treatment program will give a superior response rate and/or a longer remission duration than methotrexate alone in patients with squamous cell carcinoma of the head and neck region.

METHOD

Patients who meet the criteria as outlined in the protocol will be randomized to receive one of the following treatment plans:

Plan I: Methotrexate 15 mg/M^2 IM daily x 3 (3 week cycles)

Plan II:

Methotrexate	15 mg/M^2	IM daily x 3
Methyl CCNU	200 mg/M^2	PO day 1
Bleomycin	12.5 units/M^2	IM on days 25, 29, 32 36
	(6 week cycles)	

Dose modifications will be made as needed for each individual patient. Patients will be followed until remission or relapse in an effort to identify the duration of response within the two study arms.

PROGRESS

(77 10 - 78 09) No patients were entered on this protocol during FY 78, and it has been replaced by SWOG 7814.

During the previous year, two patients were treated on the study. One asked to be taken off the study after one month of treatment with no results, and the second was transferred to SWOG 7629 after four months of treatment with no results.

STATUS: (T)

TITLE: SWOG 7524, Chemotherapy in Stages III & IV Ovarian and Endometrial Carcinoma

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/28

TECHNICAL OBJECTIVE

Primary: 1. To compare the effectiveness of chemotherapy alone (adriamycin-cyclophosphamide) vs chemoimmunotherapy (adriamycin-cyclophosphamide plus BCG) for remission induction in patients with Stages III and IV ovarian and endometrial carcinoma who have had no previous cytotoxic chemotherapy.
2. To test the effectiveness of continued chemoimmunotherapy vs chemotherapy in maintaining complete remissions (documented) achieved during the initial 12-month induction therapy.
3. To test the effectiveness of continued chemoimmunotherapy vs chemotherapy in inducing complete remissions or maintaining partial remissions in patients with occult disease at the time of restaging for complete response or in patients achieving only partial clinical remission during the initial 12-month induction therapy.

Secondary: 1. To establish baseline and serial data on immunologic status in both chemotherapy and chemoimmunotherapy groups.
2. To evaluate systematic restaging of patients judged to be in complete clinical remission.

METHOD

Patients meeting the criteria will be randomized to two treatment plans for both remission induction and maintenance. Treatment 1 will consist of adriamycin and cytoxan; treatment 2 will consist of adriamycin and cytoxan plus BCG. For maintenance, treatment 1 will consist of cytoxan, and treatment 2 will consist of cytoxan plus BCG. Twelve courses of treatment will constitute the remission induction phase of the protocol. If residual tumor is detected following the 12 courses of therapy, BCG plus cyclophosphamide for the chemoimmunotherapy patients or cyclophosphamide alone for the chemotherapy patients may be continued at 4-week intervals until a total of 2 years of therapy has been achieved

or there is documented evidence of recurrence or progression of disease. Those patients who have no detectable postinduction disease or who have occult disease or only clinical partial responses after the initial 12 courses of induction therapy are to be continued on maintenance therapy as outlined in the protocol.

PROGRESS

(77 10 - 78 09) No patients have been registered on this protocol.

STATUS: (O)

TITLE: SWOG 7611, Cis-Platinum for Refractory Sarcomas

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/29

TECHNICAL OBJECTIVE

This study proposes to determine the efficacy of cis-diammine-dichloroplatinum (II) (NSC-119875, CACP) in the treatment of patients with advanced sarcomas refractory to adriamycin combinations.

METHOD

Patients with a biopsy confirmed diagnosis of soft tissue or bony sarcoma, who meet other criteria as specified in the protocol, will be started on the following treatment: 50 cc of 25% Mannitol is to be given as a 30-60 minute infusion followed by CACP 15 mg/M^2 IV bolus days 1-5, repeated at 28-day intervals. If there is evidence of a tumor response or acceptable stable disease, the drug will be continued at 4-week intervals indefinitely. With evidence of progression after two courses, the patient will go off study. An adequate trial will consist of two courses of chemotherapy.

PROGRESS

(77 10 - 78 09) No patients have been registered on this protocol, and it has been terminated.

STATUS: (T)

TITLE: SWOG 7624, ADR vs ADR+CACP in Transitional Cell Baldder Carcinoma

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/30

TECHNICAL OBJECTIVE

To compare the efficacy of adriamycin vs adriamycin plus cis-diamminedichloroplatinum (II) in recurrent or disseminated transitional cell bladder carcinoma.

METHOD

Patients with histologically proven transitional cell bladder carcinoma, who meet other criteria as outlined in the protocol, will be randomized to receive ADR alone or ADR+CACP. ADR will be given in a dose of 50 mg/M^2 IV on day 1 of each course for Treatment Plan I. On Treatment Plan II, adriamycin will be given in a dose of 50 mg/M^2 IV on day 1 of each course; CACP will be given in a dose of 50 mg/M^2 IV on day 2 of each course; immediately prior to the administration of CACP, the patient is to be given an IV injection of 12.5 grams of Mannitol. An adequate trial will be two courses. All patients must be observed for a minimum of six weeks. Courses will be repeated every three weeks.

PROGRESS

(77 10 - 78 09) Two patients have been entered on this protocol.

Patient I: Treated March - October 1977 (6 months) with stabilization of extensive disease for five months. Patient expired November 1977.

Patient II: Treated with two courses - good partial response which has lasted to the present time (13 months), with additional standard chemotherapy subsequently.

STATUS: (O)

TITLE: NWOG 3176, Evaluation of the Combination of Methyl-CCNU and 5-Fluorouracil vs Methyl-CCNU, 5-Fluorouracil and Vincristine in the Treatment of Metastatic or Incompletely Resected Colorectal, Gastric, and Pancreatic Adenocarcinomas.

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/32

TECHNICAL OBJECTIVE

To determine and compare the effectiveness of therapy combining Methyl-CCNU, 5-Fluorouracil plus Vincristine with the combination of Methyl-CCNU and 5-Fluorouracil with respect to objective remission and duration of remission in metastatic and imcompletely resected colorectal, gastric, and pancreatic adenocarcinoma.

To determine the duration of patient survaival and its relationship to type of therapy and response to therapy.

METHOD

Eligibility: Patients with histologically confirmed adenocarcinoma of the colon, rectum, stomach, or pancreas with surgically incurable disease, who have had no prior chemotherapy and who meet other criteria as specified in the protocol.

Patients will be randomized to either Arm I or Arm II of the study.

Arm I: Combined Methyl-CCNU, 5 FU, and Vincristine.

Drug	Day	Dosage	Route
Methyl-CCNU	1	150 mg/M^2	Oral
5 FU	1-5	350 mg/M^2	IV
5 FU	36-40	400 mg/M^2	IV
Vincristine	1 & 36	1 mg/M^2	IV

Arm II: Patients to be treated without Vincristine and will receive Methyl-CCNU and 5-FU in the dosages indicated above.

The cycle of therapy will be repeated at 10 weeks if patient's condition permits and if objective disease progression has not occurred.

NWOG 3176 - Stutz

PROGRESS

(77 11 - 78 09) Five patients were treated on this protocol; four expired and one with progressive disease has been taken off the protocol. Patients were treated for 2, 4, 5, 7, and 8 months. Three patients had slow progression and two had fairly rapid deterioration while on treatment.

The investigators have conducted this study in conjunction with the Northwest Oncology Group. This protocol has been terminated due to the termination of the Northwest Oncology Group.

STATUS: (T)

TITLE: SWOG 7613, Combination Chemotherapy for Advanced Soft Tissue Sarcomas Utilizing Adriamycin, DIC, Cyclophosphamide and Dactinomycin. Phase III.

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/34

TECHNICAL OBJECTIVE

To determine the maximal effective chemotherapy induction regimen for patients with disseminated soft tissue sarcomas who have probability of response $\geq$50%. To determine if cycling the use of adriamycin and maintenance with CY-DIC-DACT increases the duration of CR's treated initially with A-DIC.

METHOD

Patients with biopsy confirmed diagnosis of soft tissue sarcoma with evidence of metastatic disease, who meet the other criteria as outlined in the protocol, will be stratified according to adequate or inadequate marrow reserve. These groups will then be randomized to receive adriamycin + DIC; adriamycin + DIC + Cytoxan; or adriamycin + DIC + Dactinomycin, in dosages as specified in the protocol. For both adequate and inadequate bone marrow reserve patients, a complete cycle of chemotherapy shall be repeated every 22 days, counting the first day of therapy as day 1. If on day 22 the white blood count is still less than 2,000 and/or platelet count still below 75,000, the start of the next course shall be delayed until these levels have been reached. In addition a new cycle of chemotherapy shall not be initiated unless stomatitis from previous therapy has been resolved. Dose changes and continuation of treatment shall be determined on an individual patient basis.

PROGRESS

(77 10 - 78 09) No patients have been registered on this protocol.

STATUS: (O)

TITLE: SWOG 7620, Treatment of Early Squamous Cell Carcinoma of the Head and Neck with Chemotherapy or Chemoimmunotherapy Following Initial Surgery and/or Radiotherapy

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/35

TECHNICAL OBJECTIVE

To determine if the disease-free interval and survival of patients in high risk categories of squamous head and neck cancer can be improved by adjuvant chemotherapy or chemoimmunotherapy after initial surgery, radiotherapy, or combination approach have resulted in no clinically evident disease. To accumulate immunologic data in treated and untreated patients with this malignancy.

METHOD

Patients will be registered and randomized after the reaction from the initial operative or radiotherapeutic intervention has settled and when they have achieved no clinically evident disease. The randomization process must be accomplished no later than three months after the completion of the surgery or irradiation. The tumor will be stratified into one of the four broad anatomic regions: oral cavity, larynx, pharynx, nasal cavity, and paranasal sinuses. The control group will receive no further therapy after initial surgery and/or irradiation. The chemotherapy group will consist of methotrexate 12 mg/M^2 IM daily x 3 days every 21 days for one year. The chemotherapy-immunotherapy arm will consist of methotrexate 12 mg/M^2 IM daily x 3 days every 21 days for one year with BCG scarifications administered on day 8 and 14 for eight doses of BCG. Following eight doses, the BCG may then be administered on day 14 only and continued for the remainder of the year. BCG will not be applied to the neck.

PROGRESS

(77 10 - 78 09) No patients have been registered on this protocol.

STATUS: (O)

TITLE: SWOG 7629, Cis-Diamminodichloroplatinum (II) in the Treatment of Refractory Epidermoid Carcinomas of the Head and Neck Region. Phase II Study.

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/36

TECHNICAL OBJECTIVE

The purpose of this study is to determine with some degree of precision, the efficacy and toxicity of a particular program utilizing Cis-Diammine Dichloride Platinum (II) (NSC-119875, CACP) and mannitol in the treatment of diuresis patients whose epidermoid carcinomas of the head and neck region have demonstrated refractoriness to more standard chemotherapy.

METHOD

Patients who have a biopsy-confirmed diagnosis of epidermoid carcinoma of the head and neck region and meet the criteria as outlined in the protocol shall be registered on the study. The initial course will be given at a dose of 50 mg/M^2 IV by bolus both on day 1 and day 8 of the course. For subsequent courses, the dose will be modified based on the effects of the immediately previous course. All patients will receive mannitol diuresis at the time of the cis-platinum injection (bolus injection of 12.5 gm mannitol followed by 25 gm of mannitol in 1000 cc of D5W infused over two hours). The bolus of CACP will be injected into the IV line. This procedure will be repeated each time CACP is administered. Allopurinol prophylaxis should be used to prevent hyperuricemia. Therapy is to be repeated at four week intervals or as soon thereafter as the BUN level is no greater than 30 mg%, the serum creatinine no greater than 2.0 mg%, and the WBC and platelet count are above 4,000 and 150,000 respectively. As long as there is evidence of tumor regression or disease stability at an acceptable level, the drug will be continued at approximate intervals indefinitely. Disease progression after two courses of therapy will constitute an adequate trial, and the patient will be taken off study.

SWOG 7629 - Stutz

PROGRESS

(77 10 - 78 09) Three patients were treated on this protocol during FY 78.

Patient I. Partial response - 2½ months
Patient II. Partial response - 1 month
Patient III. No response after 1½ courses. Patient refused further treatment because of severe nausea and vomiting.

All these patients have expired from progressive disease.

This protocol has been terminated and replaced by SWOG 7814.

STATUS: (T)

TITLE: SWOG 7521, Adjuvant Melanoma Protocol

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/38

TECHNICAL OBJECTIVE

1. To determine the efficacy of BCNU, hydroxyurea, and imidazole carboxamide (BHD) in preventing the recurrence of disease and prolonging the survival of patients with primary malignant melanoma who have received definitive surgical treatment for their primary lesions, have no evidence of residual disease, but in whom by the clinical and pathological characteristics of the primary lesion can be predicted to have a high incidence of recurrence. 2. To determine the efficacy of combination chemotherapy (BHD) with and without BCG in preventing the development of metastases and prolonging the disease-free interval and survival of patients with recurrent malignant melanoma which has been surgically excised ("minimal residual disease"). 3. To determine the immunocompetence of patients with malignant melanoma and any correlation with prognosis. 4. To determine the influence of chemotherapy and chemoimmunotherapy upon the immunocompetence of these patients with malignant melanoma.

METHOD

Patients who have a histologically confirmed diagnosis of malignant melanoma and have not been previously treated with chemotherapy or radiation therapy and meet the other criteria as outlined in the protocol shall be entered in the study. Patients will be classified as follows for randomization: Class I - localized disease; Class II - regional and solitary distant metastatic disease. Patients with Class I disease will be randomized between BHD and no treatment. Patients with Class II disease will be randomized to either BHD or BHD + BCG. Patients will be treated for one year or until recurrent disease develops. Patients randomized to no treatment will be followed in a similar fashion. After one year of treatment patients are to remain on study and be followed on no treatment.

PROGRESS

(77 10 - 78 09) No patients have been registered on this protocol.

STATUS: (O)

TITLE: SWOG 7603, Effect of Schedule on Activity of 5-Azacytidine in Acute Leukemia. Phase III Protocol

PRINCIPAL INVESTIGATOR: LTC FRIEDRICH H. STUTZ, MC

WORK UNIT NO: 77/39

TECHNICAL OBJECTIVE

This study will compare the activity and toxicity of single dose vs continuous 5-day infusions of 5-azacytidine in patients with acute leukemia.

METHOD

Patients will be randomized to one of the following regimens:

1. Single day infusion of 750 mg/M^2. 5-azacytidine will be given in 3 divided doses (250 mg/M^2 administered in 200 ml of Ringer's lactate solution over 2 hours) at 4 hour intervals (2 hours on therapy, 2 hours off therapy).

2. Five day infusion of 300 mg/M^2/day. 5-azacytidine will be administered in 4 divided doses in 200 ml Ringer's lactate solution as a continuous infusion over each 6 hour period. Each 6 hour dose should be prepared within 2 hours before use, and preferably immediately before administration.

Courses will be repeated at 3 week intervals unless the bone marrow cellularity remains less than 10%. The dosage of subsequent courses of 5-azacytidine will be based upon the patient's response to the previous course.

PROGRESS

(77 10 - 78 09) No new patients were entered on this protocol during FY 78. One patient had been studied earlier, but expired too early (after three days) for response.

STATUS: (O)

TITLE: SWOG 7426/27, Chemoimmunotherapy for the Non-Hodgkin's Lymphomas. CHOP-Bleomycin vs CHOP + BCG vs COP + Bleomycin Induction Therapy. No Maintenance vs BCG for Maintenance

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/41

TECHNICAL OBJECTIVE

1. To compare the effectiveness of two chemotherapy regimens (CHOP + bleomycin) or chemoimmunotherapy (CHOP + BCG) for remission induction in previously untreated patients with non-Hodgkin's lymphomas.
2. To establish baseline and serial data on immunologic status in both chemotherapy and chemoimmunotherapy groups.
3. To evaluate systematic restaging of patients judged to be in complete clinical remission (CR).
4. For patients proven to be in complete remission after induction, to test the value of continued maintenance immunotherapy (BCG) vs no maintenance treatment.
5. For patients who only achieve a partial remission during induction, to test the effectiveness of continued treatment with chemoimmunotherapy.

METHOD

Patients with any histologic type of stage III or IV non-Hodgkin's lymphoma established by biopsy will be randomized to one of the three induction programs. The schema for the study is given in the protocol. Remission Induction: Eight courses of treatment will constitute remission induction. If induction results in a CR and this is confirmed by restaging, then the patient is eligible for a second randomization into the maintenance phase of this study. If residual lymphoma is detected during restaging, an additional three courses of treatment will be administered, restaging repeated, and patients in CR will be eligible after 11 courses of induction for the maintenance phase. Patients who are only in a partial remission after 11 courses of treatment are eligible for continued treatment with chemoimmunotherapy.

SWOG 7426/27 - Stutz

PROGRESS

(77 10 - 78 09) No new patients were entered on this study during FY 78. One patient had been treated earlier for 3 months with partial response.

STATUS: (O)

TITLE: SWOG 7628, Combined CT/RT/IT for Oat Cell Cancer of the Lung (Chemotherapy, Radiation Therapy, Immunotherapy).

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/46

TECHNICAL OBJECTIVE

1. To use combination chemotherapy, local radiotherapy, and maintenance chemotherapy or chemoimmunotherapy in the treatment of oat cell carcinoma of the lung in order to improve the quality of survival and the duration of survival.
2. To compare the effectiveness of two combination chemotherapy induction regimens in a randomized fashion prior to radiotherapy of the primary.
3. To test the effectiveness of continued chemoimmunotherapy vs chemotherapy in maintaining complete or partial remissions.
4. To test the effectiveness of continued immunotherapy vs no maintenance treatment in patients achieving long-term complete remissions.
5. To establish baseline and serial data on immunologic status in both chemotherapy and chemoimmunotherapy groups.

METHOD

Patients with histologically proven diagnosis of oat cell carcinoma or small cell undifferentiated carcinoma of the lung with no prior chemotherapy or radiotherapy, who meet the other criteria as outlined in the protocol, will be entered on this study. Patients will be randomized into four treatment arms with different combinations of CT, RT, and IT as specified in the treatment plan of the protocol. Cyclophosphamide, vincristine, methotrexate, 5-fluorouracil, and adriamycin are the drugs to be used. BCG vaccine will be used for immunotherapy.

PROGRESS

(77 10 - 78 09) Two patients were treated for less than one month each. Both had significant progression while on treatment.

STATUS: (O)

TITLE: M-77-1, Forty-Two Hour Methotrexate Infusions with Citrovorum Rescue - A Clinicopharmacokinetic Analysis (A Phase I-II Study).

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/48

TECHNICAL OBJECTIVE

To determine the maximal tolerated dose of methotrexate (MTX) which will maintain a constant plasma antifolate concentration for 42 hours.

To identify what clinical factors alter renal clearance of MTX.

To evaluate the antitumor effect of 42-hour MTX infusions with citrovorum.

METHOD

Patients with any cancer resistant to conventional therapy who meet the other criteria as outlined in the protocol will enter the study in sequence, four patients being treated at each plasma MTX level as outlined in the protocol. A course of treatment will consist of a priming dose of MTX over the first hour, an infusion of MTX over the subsequent 41 hours, and citrovorum factor rescue thereafter, beginning at the time MTX is discontinued. Courses are repeated every two weeks.

At Madigan Army Medical Center this treatment is being used only in patients with tumors that have shown response to it, e.g., sarcoma.

PROGRESS

(77 10 - 78 09) Two patients have been treated on this protocol.

Patient I: Adjuvant therapy for osteogenic sarcoma - complete response (no recurrence) for 19 months.

Patient II: Treatment for squamous cell carcinoma of the lung for one month (2 courses) - progressive disease while on study.

STATUS: (O)

TITLE: SWOG 7630, Protocol for Chemotherapy of Advanced Prostatic Cancer (Stage D), Phase III

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/51

TECHNICAL OBJECTIVE

1. To compare the rate of response of hydroxyurea to a two-drug combination of adriamycin and cyclophosphamide in patients with advanced carcinoma of the prostate who have measurable disease (Stage D - bone metastases or extra-pelvic disease).
2. To compare the duration of survival in patients with nonmeasurable disease treated with one of the treatment regimens.
3. To estimate the response rate to each crossover regimen in patients that have been treated and did not respond to one of the regimens.

METHOD

Patients with advanced Stage D prostatic cancer (disease in bone or other extra-pelvic site) who have not received any of the protocol agents and who meet the other criteria as listed in the protocol will be randomized to Treatment #1 (hydroxyurea) or Treatment #2 (adriamycin and cyclophosphamide) with dosages as outlined in the protocol. Failure on either of the treatment programs will result in crossover to the other program. Progression as defined in the protocol may occur as early as one treatment course or 3 weeks of hydroxyurea.

PROGRESS

(77 10 - 78 09) No patients have been registered on this protocol.

STATUS: (T)

TITLE: SWOG 7518, Stage III A and B Hodgkin's Disease Remission Induction by Radiation Therapy Plus Chemotherapy Combination versus Chemotherapy Alone. Phase III

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/52

TECHNICAL OBJECTIVE

1. To compare the effectiveness of 10 courses of a five-drug combination chemotherapy (including nitrogen mustard, vincristine, procarbazine, prednisone, and bleomycin) program against the combined three courses of chemotherapy followed by total nodal irradiation therapy program for complete remission induction in patients with Stage III asymptomatic -A or symptomatic -B disease.
2. To evaluate the systematic "restaging" of patients in apparent complete remission.
3. To assess the length of unmaintained remission after intensive induction with ten courses of chemotherapy treatment versus the combination chemoradiation therapy, after documentation of complete remission status by careful "restaging".
4. To assess the toxicity of the chemotherapy alone portion of the study versus the toxicity of the combination of chemotherapy and radiation therapy.
5. To intercompare the results of this program with those to be obtained by SWOG 7406 (ongoing).

METHOD

Patients with any histopathologic type Stage III Hodgkin's disease and no prior chemotherapy or radiation therapy who meet the other criteria as outlined in the protocol will be randomized to either Treatment 1 or Treatment 2. Treatment 1: chemotherapy alone (nitrogen mustard, vincristine, procarbazine, and prednisone plus bleomycin). Treatment 2: chemotherapy plus radiation therapy (chemotherapy as above followed by total nodal radiotherapy). At the completion of ten courses of chemotherapy or of the total combination chemotherapy, radiation therapy program, a thorough evaluation for evidence of persistent Hodgkin's disease is required. If complete remission is confirmed by this evaluation, no further treatment will be given until relapse occurs. If remission is not confirmed, appropriate treatment will be given on an individual basis.

SWOG 7518 - Stutz

PROGRESS

(77 10 - 78 09) One patient has been treated on this protocol for one year and is in complete remission.

STATUS: (O)

TITLE: SWOG 7433, Non-Hodgkin's Lymphomas (Stages I, I_E, II and II_E). A Phase III Study

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/53

TECHNICAL OBJECTIVE

To compare the remission rate, remission duration, and survival in patients with non-Hodgkin's lymphoma, pathologic stages I, I_E, II and II_E treated with extended field radiotherapy (supra-diaphragmatic mantle or abdominal field) alone or with extended field radiotherapy plus combination chemotherapy (Cytoxan, Hydroxyl-daunorubicin(adriamycin), Oncovin (vincristine), and prednisone).

METHOD

Patients newly diagnosed (no type of prior therapy) with non-Hodgkin's lymphoma except mycosis fungoides and diffuse lymphocytic well differentiated lymphoma will be thoroughly evaluated for extent of disease and then randomized to either radiation therapy or radiation therapy plus chemotherapy. If the patient does not achieve a complete remission after completion of his treatment course, he will be removed from the study. Those achieving complete remission will be followed for two years or until relapse.

PROGRESS

(77 10 - 78 09) One patient has been treated on this protocol. The patient has a complete response 95 days after beginning of treatment.

STATUS: (O)

TITLE: SWOG 7406, Advanced Hodgkin's Disease: Remission Induction (MOPP #5). Phase III.

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/54

TECHNICAL OBJECTIVE

1. To compare the effectiveness of two MOPP (nitrogen mustard, vincristine, procarbazine, and prednisone) + bleomycin + adriamycin combinations against MOPP + bleomycin for remission induction in patients with advanced Hodgkin's disease without prior chemotherapy.

2. To evaluate systematic restaging of patients in apparent complete remission.

3. To assess the length of unmaintained remission after intensive induction with ten courses of treatment and after documentation of complete remission (CR) status by careful restaging.

4. To evaluate by crossover design the remission induction potential of the other study combinations for patients who relapse during unmaintained remission.

METHOD

All previously untreated patients with Ann Arbor Stages III B or IV A+B Hodgkin's disease who meet the other criteria as outlined in the protocol will be randomized to one of the induction programs as specified in the protocol. Ten courses of treatment at 4-week intervals will constitute remission induction. If induction results in a CR and this is confirmed by restaging, then no further treatment will be given. If at least a partial remission is indicated, another four courses will be administered in a second attempt to achieve a CR. Persistence of disease after 14 courses will constitute an induction failure and the patient will be taken off study. Relapsing patients will be crossed over to one of the other induction combinations.

PROGRESS

(77 10 - 78 09) One patient treated for 19 months is in complete remission. This protocol has been replaced by SWOG 7808.

STATUS: (T)

TITLE: SWOG 781, Phase III Protocol - Radiotherapy-Chemotherapy (MOPP) for Stages I and II, A and B Hodgkin's

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/55

TECHNICAL OBJECTIVE

To compare total nodal radiotherapy (TN-XRT) or "mantle" and para-aortic radiotherapy to involved field radiotherapy (IF-XRT) plus MOPP (nitrogen mustard, vincristine, prednisone, and procarbazine) chemotherapy in patients with stages I and II, A and B disease.

METHOD

Patients with biopsy-proven Hodgkin's disease who have received no prior chemotherapy or radiotherapy and who meet other criteria as outlined in the protocol will be randomized to one of two treatment programs: (1) TN-XRT; (2) IF-XRT followed by MOPP chemotherapy. Following completion of the IF-XRT, a rest period of four weeks will be interposed before chemotherapy is started. Dosages for chemotherapy and radiotherapy and length of courses of treatment as specified in the protocol.

PROGRESS

(77 10 - 78 09) No patients have been registered on this protocol.

STATUS: (O)

TITLE: SWOG 7618, Combined Preoperative Adjuvant Therapy in Rectal Carcinoma

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/58

TECHNICAL OBJECTIVE

1. To determine if adjuvant preoperative irradiation and combination chemotherapy will yield a higher incidence than expected of Duke A lesions in a high risk group of patients with rectal carcinoma.
2. To determine the survival of patients with rectal carcinoma, both those with and without regional node metastasis, following the combined treatment stated in #1.

METHOD

Patients with histologically proven carcinoma of the rectum who meet the other criteria as listed in the protocol will be randomized to one of two treatment modalities: (1) radiotherapy followed by surgery; (2) radiotherapy and chemotherapy followed by surgery. For both treatment arms, the preoperative irradiation and surgery will be identical. Radiotherapy: 2000 rads at the rate of 1000 rads per week, five treatments per week. Chemotherapy: mitomycin-C, 10 mg/M^2, given once IV through a running IV as a bolus injection, or a 20-30 minute infusion; 5-fluorouracil 1000 mg/M^2/day as a continuous 24 hour infusion via a central venous pressure indwelling intracath for 4 days. Both 5-fluorouracil and mitomycin will be started on the first day within eight hours of the completion of the first radiation treatment. The 4-day 5-fluorouracil administration will be repeated starting on day 28. The patient will undergo an abdominoperineal resection 6-8 weeks after completion of the radiotherapy.

PROGRESS

(77 10 - 78 09) One patient has been treated on this protocol for 18 months with complete remission.

STATUS: (O)

TITLE: SWOG 7619, Evaluation of Ftorafur in the Treatment of Metastatic Adenocarcinoma of the Colon and Rectum, Phase II.

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/59

TECHNICAL OBJECTIVE

To determine the efficacy of Ftorafur in disseminated adenocarcinoma of the colon and rectum.

METHOD

Patients who have biopsy proven adenocarcinoma arising from the colon or rectum who meet other criteria as outlined in the protocol will be entered on the protocol in two categories (with or without liver metastasis) for evaluation purposes. Dose schedule: Ftorafur 2.25 gm/M^2 over a 2-hour infusion daily for 5 days. Reconstituted solution may be administered in 250 cc of 5% dextrose/normal saline. Repeat courses every 21 days provided patient has recovered from toxicity from the previous course. Adequate trial consists of two courses of therapy.

PROGRESS

(77 10 - 78 09) One patient was treated for nine months on this protocol. He had slowly progressive disease while on treatment.

STATUS: (T)

TITLE: SWOG 7622, Combined Modality for Mycosis Fungoides -- Stage I (Phase II)

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/60

TECHNICAL OBJECTIVE

1. To compare the effectiveness of combined electron beam therapy and adjuvant chemotherapy vs electron beam therapy alone for patients with Stage I mycosis fungoides to determine the time to recurrence and to determine the percentage of recurrence.
2. To determine the effectiveness of adjuvant chemotherapy and survival patterns of such patients.
3. To determine the value of staging laparotomy in the management of mycosis fungoides.

METHOD

Patients who have two or more skin biopsies read as mycosis fungoides by a pathology panel and who meet other criteria as listed in the protocol will be randomized to receive electron beam therapy alone or electron beam therapy and adjuvant chemotherapy. Electron beam total body irradiation will be given via the Stanford Technique to a dose of 3000-5000 rads/40-60 days. Following the completion of electron beam therapy a rest period of four weeks is completed before chemotherapy is started. Chemotherapy will consist of: Cytoxan, 450 mg/M^2 IV on day 1 only; adriamycin, 30 mg/M^2 on day 1 only; vincristine, 1.4 mg/M^2 on day 1; prednisone, 100 mg orally for 5 days; and bleomycin, 2 units/M^2 IV 30" after vincristine on day 1. A total of 8 cycles at 3-week intervals will be delivered. Patients will be followed indefinitely or to a point of relapse.

PROGRESS

(77 10 - 78 09) No patients have been registered on this protocol.

STATUS: (O)

TITLE: SWOG 7625, Combination Chemotherapy for Advanced Sarcomas of Bone and Mesothelioma Utilizing Rubidazone and DIC (Dimethyl Triazeno Imidazole Carboxamide)

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/61

TECHNICAL OBJECTIVE

1. To determine the efficacy in terms of rate of response of combination chemotherapy with the 2-drug regimen RubiDIC (Rubidazone + DIC) in patients with metastatic sarcomas of bone and mesothelioma.
2. To determine the duration of remission and survival pattern of patients on this study and compare them with that of patients with metastatic bone sarcomas and mesothelioma on previous Southwest Oncology Group or M.D. Anderson Hospital protocols using adriamycin containing regimens.
3. To determine the toxicity of the regimen especially with regard to cardiac toxicity.

METHOD

Patients with a biopsy-confirmed diagnosis of bony sarcoma or mesothelioma with measurable metastases who have already received appropriate surgical therapy, who have not received prior adriamycin, daunorubicin, rubidazone, DIC, or BIC, and who meet other criteria as outlined in the protocol will be entered in the protocol on two treatments. Treatment I (adequate marrow reserve) will consist of rubidazone, 150 mg/M^2 IV on day 1 and DIC, 250 mg/M^2/day IV on days 1-5 inclusive. Treatment II (inadequate marrow reserve) will consist of rubidazone, 120 mg/M^2 IV on day 1 and DIC, 200 mg/M^2/day IV on days 1-5 inclusive. For both treatments, a complete cycle of chemotherapy shall be repeated every 22 days. Patients who remain in complete remission having received a total of two years of chemotherapy will have the chemotherapy discontinued, but will continue to be followed.

PROGRESS

(77 10 - 78 09) No patients have been registered on this protocol.

STATUS: (O)

TITLE: SWOG 7626, ROAP Induction Chemotherapy of Acute Leukemia in Patients Over the Age of 50

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/62

TECHNICAL OBJECTIVE

To determine the efficacy of the 4-drug combination chemotherapy regimen ROAP (rubidazone, vincristine, arabinosyl cytosine, and prednisone) in remission induction chemotherapy in patients with acute leukemia over the age of 50. To determine the toxicity of the regimen.

METHOD

Patients age 50 or greater with a diagnosis of acute leukemia who have received no extensive prior therapy who meet other criteria as outlined in the protocol will be divided into two groups: Group I - a circulating blast count of less 30,000; Group II - a circulating blast count $\geq$30,000/cu ml. Both groups will receive identical treatment: rubidazone, 200 mg/M^2, IV on day 1; vincristine, 2 mg IV day 1; arabinosyl cytosine, 70 mg/M^2, continuous IV infusion days 1-7; and prednisone, 100 mg, PO qd days 1-5. Courses repeated approximately every 20 days. Patients showing response more than 50% reduction in leukemic infiltrate after three courses will receive chemotherapy as long as improvement persists. When subsequently progressive disease follows, patients will be removed from study. Separate protocols will be devised for maintenance therapy.

PROGRESS

(77 10 - 78 09) One patient was on treatment for one course (3 weeks) with no response. The patient was transferred out for WBC transfusion and possible marrow transplant, but died approximately three weeks later.

STATUS: (T)

TITLE: SWOG 7632, Combined Modality Protocol for Recurrent Breast Cancer, Phase III

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/63

TECHNICAL OBJECTIVE

1. To establish the survival of breast cancer patients when treating the first recurrence with a coordinated hormonal chemotherapeutic approach.

2. To determine the efficacy of a response to the antiestrogen Tamoxifen in predicting response to ablative surgery.

3. To correlate hormonal manipulations with estrogen and progesterone receptors where possible.

METHOD

First recurrence patients who have been surgically and/or radiotherapeutically treated with the intent of cure of their primary disease and who meet other criteria as outlined in the protocol will be divided into two groups. Group I (no prior castration) will receive Tamoxifen, 10 mg BID, followed by castration plus Tamoxifen. Responding patients will subsequently undergo adrenalectomy or hypophysectomy; nonresponding patients will receive chemotherapy. Group II (prior castration) will start on Tamoxifen. Responding patients will after relapse go directly to adrenalectomy or hypophysectomy; nonresponding patients will go directly to chemotherapy. Surgical guidelines and chemotherapy as outlined in protocol.

PROGRESS

(77 10 - 78 09) Two patients have been treated on this protocol.

Patient I: on treatment 8+ months - stable disease.

Patient II: On treatment 4 months. Mixed response - decrease of chest wall nodules; development of pericardial metastasis. Patient died five months after she was taken off the protocol with progressive disease.

STATUS: (O)

TITLE: SWOG 7633, A Study of Rubidazone (NSC 164011) in Adults with Previously Treated Acute Leukemia and in Patients with CML Blast Transformation. Phase II.

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/64

TECHNICAL OBJECTIVE

1. To determine the efficacy of rubidazone in adult patients with previously treated acute leukemia and in patients with CML blast transformation.

2. To determine the toxicity of the drug in the above patients, with special reference to patients having prior therapy with adriamycin.

METHOD

Adult patients with acute leukemia having had prior chemotherapy and patients with CML blast transformation will be entered on the study, if other criteria as outlined in the protocol are met. Starting dosage - Day 1: good risk patients - 450 mg/M^2 IV; poor risk (over age 50 and infected or with less than 50% leukemia infiltrate) - 300 mg/M^2 IV. Subsequent doses and time intervals between doses will be determined by individual progress as outlined in the protocol. Maintenance doses of approximately 150 mg/M^2 of rubidazone may be given every three weeks after remission is reached. At the termination of rubidazone treatment, patients in remission will be maintained in the fashion deemed appropriate by the investigator.

PROGRESS

(77 10 - 78 09) One patient was treated for two courses in the past year with a partial response for one month. In the previous year, one patient was entered on protocol and expired shortly thereafter.

STATUS: (T)

TITLE: SWOG 7634, Evaluation of MeCCNU Plus B-2'-Deoxythioguanosine and Mitomycin-C Plus B-2'-Deoxythioguanosine in the Treatment of Refractory Disseminated Colorectal Carcinoma. Phase III Study

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/65

TECHNICAL OBJECTIVE

1. To evaluate the effectiveness of MeCCNU plus B-2'-deoxythioguanosine (BTGdR) for remission induction in disseminated colorectal carcinoma for patients failing to respond or relapsing from chemotherapy with Mitomycin-C plus 5-FU or Mitomycin-C plus Ftorafur, 5-FU alone, or Ftorafur alone.
2. To evaluate the effectiveness of MITO-C plus BTDdR for remission induction for patients failing to respond or relapsing from chemotherapy with MeCCNU plus 5-FU of MeCCNU plus Ftorafur, 5-FU alone, or Ftorafur alone.

METHOD

Patients with histologically proven disseminated colorectal carcinomas who meet the other criteria as outlined in the protocol will be treated as follows:

Treatment 1: Patients with prior exposure to MeCCNU + 5 FU or MeCCNU + Ftorafur, 5-FU alone or Ftorafur alone.

Good risk: MITO-C, 15 mg/M^2 IV days 1 and 56
BTGdR, 60 mg/M^2 days 1-5, 28-32, 56-60

Poor risk: MITO-C, 10 mg/M^2 IV on days 1 and 56
BTGdR, 50 mg/M^2 on days 1-5, 28-32, 56-60

Treatment 2: Patients with prior exposure to Mitomycin-C + 5-FU or Mitomycin + Ftorafur, 5-FU alone or Ftorafur alone.

Good risk: MeCCNU, 130 mg/M^2 PO on days 1 and 56
BTGdR, 60 mg/M^2 on days 1-5, 28-32, 56-60

Poor risk: MeCCNU, 100 mg/M^2 PO on days 1 and 56
BTGdR, 50 mg/M^2 on days 1-5, 28-32, and 56-60

Patients without prior exposure to MeCCNU or Mitomycin-C will be randomized to receive Treatment I or Treatment II.

SWOG 7634 - Stutz

PROGRESS

(77 10 - 78 09) Four patients were treated for 2, 3, 5, and 6 months respectively. All patients had progressive disease while on treatment. The first patient expired.

STATUS: (O)

TITLE: SWOG 7639, Two Adriamycin, Mitomycin C and 5-Fluorouracil Combinations in the Management of Gastric Adenocarcinoma. A Phase III Study

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/66

TECHNICAL OBJECTIVE

1. To determine and to document both the response rates and the toxicities of two different combinations of adriamycin, mitomycin C and 5-fluorouracil in the management of surgically incurable adenocarcinoma of the stomach.
2. To compare the effectiveness of these two regimens.

METHOD

Patients who have unresectable gastric adenocarcinoma and an objectively measurable lesion with no prior exposure to adriamycin, daunomycin, mitomycin C, or porfiromycin, and who meet other criteria as outlined in the protocol will be randomized to one of the two treatments.

Treatment 1: sequential regimen
adriamycin, 50 mg/M^2 day 1
mitomycin C, 10 mg/M^2 day 3
5-fluorouracil, 600 mg/M^2 day 29

Treatment 2: simultaneous regimen
adriamycin, 30 mg/M^2 per dose, day 1 and 19
mitomycin, 10 mg/M^2 day 1
5-fluorouracil, 600 mg/M^2 per dose, day 1,8,29, 36

Although one single course of therapy (8 weeks on study) would be considered as an adequate trial, an attempt should be made to administer at least two courses of therapy where possible. Patients whose disease has remained stable or has regressed on therapy will be continued on this combination for a total of two years unless the adriamycin dose limitation or drug toxicity precludes such continuation of therapy.

SWOG 7639 - Stutz

PROGRESS

(77 10 - 78 09) One patient was entered on the protocol for four months with progressive disease while on treatment.

STATUS: (O)

TITLE: SWOG 7703, Radiation Therapy in Combination with BCNU, Dimethyl Triazeno Imidazole Carboxamide (DTIC) or Procarbazine in Patients with Malignant Gliomas of the Brain. Phase III

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/74

TECHNICAL OBJECTIVE

To compare the effectiveness of radiation therapy plus BCNU, radiation therapy plus DTIC, and radiation therapy plus procarbazine for remission induction, duration of remission, and survival in patients with malignant gliomas of the brain.

METHOD

Patients with histologically confirmed primary central nervous tumors of the following histologic types will be entered on the study: astrocytoma, grades 3 and 4 (glioblastoma multiforme). Other criteria: surgery with histologic diagnosis within the prior four weeks and no prior chemotherapy of any type with the exception of corticosteroids. Patients will be randomly allocated to one of the three programs: (1) radiation therapy plus BCNU; (2) radiation therapy plus procarbazine; (3) radiation therapy plus DTIC (dosage as outlined in the protocol). Since survival time is an important end point of this study, each investigator will be required to follow each patient until death and to report the death.

PROGRESS

(77 10 - 78 09) No patients have been entered on this protocol.

STATUS: (O)

TITLE: SWOG 7704, Chemoimmunotherapy for Multiple Myeloma - VMCP + VCAP vs VMCP-VBAP vs MP for Remission Induction Therapy: VMCP vs VMCP + Levamisole for Maintenance After Remission Induction. Phase III

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/75

TECHNICAL OBJECTIVE

1. To compare the effectiveness of three intermittent pulse chemotherapy combinations, VMCP + VCAP vs VMCP + VBAP vs MP for induction of remissions in previously untreated patients with multiple myeloma. (V = vincristine, M = melphalan, C = cyclophosphamide, P = prednisone, A = adriamycin, B = BCNU, L = levamisole) Results will also be compared with other combination chemotherapy treatments in previous SWOG studies, especially VMCP treatment in SWOG 7418 and previous studies of MP combinations.
2. For patients proven to have at least a 75% tumor regression after induction, to compare the value of 12 months of chemoimmunotherapy maintenance VMCP + Levamisole in comparison to VMCP alone.
3. To establish baseline and serial data on immunologic status in these patient groups.

METHOD

Patients with previously untreated multiple myeloma who meet other criteria as outlined in the protocol will be randomized to one of the following treatments. For induction:

Treatment 1: regular alternating combinations VMCP (1 cycle) then VCAP (1 cycle) alternating q 3 weeks
Treatment 2: sequential alternating combinations VMCP (3 cycles) then VBAP (3 cycles)
Treatment 3 single combination - MP 3 week cycles

For maintenance:
Treatment 1: VMCP
Treatment 2: VMCP + Levamisole

Patients still in remission at the end of 12 months of maintenance with either VMCP or VMCP plus levamisole will be followed in an unmaintained remission state. Upon relapse from unmaintained

remission, patients should be reinduced with the previously used maintenance treatment and this program should be continued until relapse.

PROGRESS

(77 10 - 78 09) Two patients have been entered on this protocol.

Patient I: On treatment 13+ months - in complete remission.

Patient II: On treatment 6 months - partial remission.

STATUS: (O)

TITLE: SWOG 7522, Chemotherapy, Splenectomy With or Without Immunotherapy in the Treatment of Chronic Myelogenous Leukemia. Phase III

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/78

TECHNICAL OBJECTIVE

To study the effects of chemotherapy, splenectomy, and/or immunotherapy on leukemic cytogenetics, immune status, appearance of blastic transformation, and any influence in overall survival.

a. To treat and control the early benign phase of chronic myelogenous leukemia with cytoxan, cytosine arabinoside, vincristine and prednisone and to study the influence of chemotherapy on bone marrow morphology, cytogenetics, and leukocyte alkaline phosphatase.

b. To study nonspecific cell mediated immunity prior to and following therapy.

c. To determine if immunotherapy with BCG will augment general immunocompetence of CML patients.

d. To remove extra tumor burden, avoid possible complication of splenic infarction and hypersplenism through surgical splenectomy.

METHOD

Splenectomy for patients entering this study will be elective. Within each group (splenectomy or no splenectomy) patients will be randomized to receive chemotherapy alone or chemotherapy + BCG immunotherapy. Hence, there will be four groups of patients.

Induction Treatment:

Treatment 1: Cytosar 100 mg/M^2 day x 5, subcutaneous
Oncovin 1.0 mg IV day 1
Cytoxan 500 mg/M^2 IV day 1
Prednisone 100 mg PO day x 5
Tice BCG scarification on days 8 and 15

Treatment 2: COAP only (same dosages as for Treatment 1)

Following three courses of induction treatment, patients will be evaluated for splenectomy. For patients not undergoing splenectomy, maintenance chemotherapy will be initiated. Splenectomy will be planned during days 21-28 after COAP #3, when the peripheral

circulating WBC is between 5 and 20,000/mm^3.

Maintenance Treatment

Treatment 1: Hydroxyurea PO in 4 divided dosages daily.
Dosage depends upon the WBC.
BCG weekly between hydroxyurea courses.

Treatment 2: Hydroxyurea PO in 4 divided dosages daily.

PROGRESS

(77 10 - 78 09) One patient was entered on this protocol and expired the day after entry.

In the previous year, one patient was treated for eight days before he expired.

STATUS: (O)

TITLE: SWOG 7635, Combined Modality Treatment of Limited Squamous Carcinoma of the Lung. Phase III.

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/82

TECHNICAL OBJECTIVE

1. To determine whether chemotherapy with adriamycin and/or immunotherapy with levamisole improve median survival of split-course radiotherapy used alone in the treatment of patients with limited extent squamous bronchogenic carcinoma.

2. To determine the qualitative and quantitative toxicity of each treatment regimen.

METHOD

Patients with a histologically confirmed diagnosis of limited squamous carcinoma of the lung with no previous chemotherapy or radiation therapy will be randomized to one of the following regimens:

Regimen A: Radiation therapy plus levamisole.
Regimen B: Radiation therapy plus adriamycin.
Regimen C: Radiation therapy plus adriamycin and levamisole.
Regimen D: Radiation therapy alone.

PROGRESS

(77 10 - 78 09) No patients entered on this protocol during FY 78. In the previous year, one patient was registered, but was never treated because he was found, on tomograms, to have metastatic disease after registration, but before the start of treatment.

STATUS: (O)

TITLE: SWOG 7701, CCNU, Ifosfamide, Adriamycin (CIA) vs. Ifosfamide - Adriamycin vs. Ifosfamide in Extensive Non-Oat Cell Lung Cancer with Methotrexate Added to Maintenance. Phase III Study.

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/83

TECHNICAL OBJECTIVE

1. To determine if ifosfamide, adriamycin, and CCNU is a more effective combination than ifosfamide alone or in combination with adriamycin in the treatment of patients with extensive non-oat cell carcinoma of the lung who are not eligible for curative radiotherapy.

2. To measure the relative efficacy of this regimen on survival.

3. To determine the qualitative and quantitative toxicity of the regimen.

4. To compare response induction.

METHOD

Eligibility criteria: All patients with a histologically confirmed diagnosis of extensive non-oat cell carcinoma of the lung, provided they have received no previous chemotherapy.

Stratification by - prior x-ray therapy; then by Karnofsky Performance Status. The patients will be randomized within each of the six stratification groups to receive on of the three treatments:

Treatment 1 - Ifosfamide 1 gm/M^2 days 1-5, then once weekly
Adriamycin 40 mg/M^2 day 2, then once q 3 weeks
CCNU 65 mg/M^2 PO day 3, then once q 8 weeks

Treatment 2 - Ifosfamide 1 gm/M^2 days 1-5, then once weekly
Adriamycin 40 mg/M^2 day 2, then once q 3 weeks

Treatment 3 - Ifosfamide 1 gm/M^2 days 1-5, then once weekly

Ascorbic acid is given 250 mg PO tid and 500 mg hs during the loading course and 250 mg tid on the days of ifosfamide therapy during maintenance.

SWOG 7701 - Stutz

Maintenance Therapy: Maintenance therapy begins 3 weeks after the last dose of adriamycin (cummulative dose of 450 mg/M^2). Ifosfamide continues to be given weekly. CCNU continues to be given every 8 weeks. Methotrexate is given in a dose of 30 mg/M^2 i.m. and repeated every 4 weeks.

PROGRESS

(77 10 - 78 09) One patient was treated with ifosfamide for one month and had pregressive disease while on treatment.

STATUS: (O)

TITLE: SWOG 7299, Clinical Trial of Radiotherapy and Chemotherapy (Cyclophosphamide, Vincristine, Acto-Dactinomycin, and Adriamycin) in Managing Non-Metastatic Ewing's Sarcoma

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/89

TECHNICAL OBJECTIVE

To compare the time interval from clinically localized tumor to appearance of metastases using irradiation of the primary tumor plus systemic chemotherapy or irradiation of the primary tumor plus chemotherapy plus bilateral pulmonary irradiation. To document (a) incidence and time of appearance of local recurrence; (b) the pattern of organ metastases so that future studies will result in programming improved means of therapy; and (c) the total survival time of patients treated by both regimes.

METHOD

Patient eligibility: all patients with tissue diagnosis of Ewing's sarcoma and no prior therapy and in whom the tumor is localized and the patient is free of demonstrable metastases. Regional involvement, specifically, malignant cells in the spinal fluid, ascitic fluid, and pleural fluid as well as nodal involvement, will be considered metastic.

Treatment: Patients will receive one of two regimens:

Regimen I: Weeks 1-6, irradiation plus vincristine and Cytoxin; Weeks 7-9, rest; Week 10, Dactinomycin; Week 11, rest; Weeks 12-15, vincristine and Cytoxin; Week 16, vincristine and Cytoxin plus adriamycin; Week 17-18, rest.

Regimen II: The same as Regimen I with the addition of bilateral pulmonary irradiation in weeks 4, 5, and 6.

Weeks 10-18 will be repeated eight times to complete the full course of treatment.

PROGRESS

(77 11 - 78 09) No patients have been entered on this study.

STATUS: (O)

TITLE: SWOG 7713/14, Chemoimmunotherapy in Non-Hodgkin's Lymphoma CHOP vs CHOP + Levamisole vs CHOP + Levamisole + BCG for Remission Induction Therapy: Levamisole vs No Maintenance after Remission Induction

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 78/02

TECHNICAL OBJECTIVE

1. To compare the effectiveness, in terms of rate of response of two chemoimmunotherapy regimens (CHOP + levamisole vs CHOP + levamisole + BCG) against CHOP for remission induction in previously untreated patients with non-Hodgkin's lymphoma.
2. For patients proven to be in complete remission after induction, to compare the duration of documented complete response obtained by continued maintenance immunotherapy with levamisole vs no maintenance therapy.
3. For patients with imparied cardiac function (not eligible for treatment with adriamycin), with mycosis fungoides, or with only a partial response to 11 courses of treatment with CHOP-levamisole + BCG, to estimate the complete response rate obtained by continued chemoimmunotherapy with COP + levamisole.
4. To estimate the CNS relapse rate in patients with diffuse lymphomas when CNS prophylaxis with intrathecal cytosine arabinoside is used.
5. To continue to evaluate the impact of systematic restaging of patients judged to be in complete remission and the value of expert hematopathology review of diagnostic material from all cases.
6. To establish baseline and serial data on immunologic status in both chemoimmunotherapy groups.

METHOD

Patients with a diagnosis of non-Hodgkin's lymphoma established by biopsy with no prior chemotherapy are eligible. Patients with chronic lymphocytic leukemia are ineligible. Patients with preexisting cardiac diasease or mycosis fungoides are ineligible for the CHOP programs, but will be treated with COP + levamisole. Patients will be stratified according to nodular or diffuse histologies, adequate or imparied bone marrow reserves, presence or absence of bone marrow involvement, and performance status. Initial drug doses are based on bone marrow reserve. Treatment plans as outlined in the protocol.

SWOG 7713/14 - Stutz

PROGRESS

(77 12 - 78 09) No patients were entered on this study.

STATUS: (O)

TITLE: SWOG 7706, Combination Chemotherapy for Stages III and IV Ovarian Carcinoma Resistant to Adriamycin-Cyclophosphamide Treatment of Single Alkylating Agent Treatment

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 78/08

TECHNICAL OBJECTIVE

1. To use a combination of 5-FU, hexamethylmelamine, and platinum in an attempt to induce complete and partial clinical remissions in patients with stages III and IV ovarian carcinoma which have failed to respond to or have relapsed following remission from adriamycin-cyclophosphamide therapy.

2. To use a combination of 5-FU, hexamethylmelamine, platinum, and adriamycin to induce complete and/or partial remissions in patients with stages III and IV ovarian carcinoma who have failed on or relapsed from previous alkylating agent therapy.

METHOD

Patient Eligibility: (1) diagnosis of ovarian carcinoma established by biopsy; epithelian type neoplasms to be included; (2) only patients with pathologic stages III or IV ovarian carcinoma are eligible; patients who have relapsed after initial radiation therapy will not be eligible; (3) only patients who had previously received and had failed or relapsed following adria-CTX therapy or those having previous single alkylating agent chemotherapy will be eligible; (4) patients with a history of serious cardiac arrhythmias, myocardial infarction, or congestive heart failure will be ineligible to receive adriamycin and should be placed on the three drug regimen (cis-platinum, hexamethylmelamine, 5-FU); (5) patients with serum creatinines >1.5 mg%, BUN's >25 mg%, and creatinine clearances of <60 mg/min or obstruction to the ureters seen on IVP are ineligible for cis-platinum and should be placed on adriamycin, 5-FU, and hexamethylmelamine where appropriate; (6) measurable residual tumor is required for entry; (7) WBC must be >2,500 and platelets >100,000/mm. BUN should be 25 mg%, and serum creatinine <1.5mg%. Creatinine clearance of $\geq$60 and no obstruction to the ureters by IVP.

SWOG 7706 - Stutz

Initial drug doses will be based on bone marrow reserve.

Treatment 1: Patients who have failed to respond to or relapsed from prior adriamycin-CTX.

5-fluorouracil	400 mg/M^2 IV on days 1 & 8
hexamethylmelamine	150 mg/M^2 PO daily days 1-14
plus pyridoxine	50 mg qd days 1-14
cis-platinum	50 mg/M^2 IV infusion (1 mg/min) day 1

Treatment 2: Patients who have previously failed on or have relapsed following therapy with single alkylating agent therapy.

adriamycin	25 mg/M^2 IV on day 1
5-fluorouracil	300 mg/M^2 IV days 1 & 8
hexamethylmelamine	150 mg/M^2 PO days 1-14
plus pyridoxine	50 mg qd, days 1-14
cis-platinum	50 mg/M^2 (1 mg/min) day 1

PROGRESS

(78 02 - 78 09) One patient was on treatment for eight months with good partial remission.

STATUS: (O)

TITLE: SWOG 7719, Addition of DDP and Bleomycin to VBAP in Relapsing and Resistant Myeloma Patients. Phase II.

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 78/09

TECHNICAL OBJECTIVE

To evaluate the frequency, degree, and duration of response with cis-platinum (DDP) and bleomycin added to vincristine-BCNU-adriamycin-prednisone combination (VBAP) in myeloma patients who failed to respond or relapsed to combinations of melphalan and/or cyclophosphamide with prednisone (M/C+P); and to compare results with previous SWOG trials of VBAP in such patients.

METHOD

Patient Eligibility: diagnosis of multiple myeloma with evidence of progressive disease and evidence of reasonable cardiac, renal, and pulmonary function, but no longer responding to or have not responded to M/C+P; a minimum granulocyte count of 1500 and a platelet count of 100,000 unless bone marrow studies indicate that the neutropenia and/or thrombocytopenia are due to far advanced myeloma and not myelotoxicity from previous treatment. Chemotherapy should be started simultaneously with maximum efforts to reverse all complications. Chemotherapy should not be started until the investigator is assured that the patient has recovered from prior radiation or drug induced myelotoxicity.

Stratification: M/C + P response then relapse patients
M/C + P no response patients

Treatment plan:

DAY	1	2	3	4	5
vincristine (total) IV	1				
BCNU IV mg/M^2	30				
adriamycin IV mg/M^2	30				
prednisone PO mg/M^2	60	60	60	60	60
bleomycin (total) IM		7.5	7.5	7.5	7.5
DDP (total) IV		20	20	20	20

Courses to be repeated every three weeks depending on bone marrow recovery. The interval between courses should not be greated than 6 weeks. Minimum number of courses for evaluation is 3; maximum number is 6.

SWOG 7719 - Stutz

PROGRESS

(78 02 - 78 09) No patients have been entered on this study.

STATUS: (O)

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TITLE: SWOG 7726, Chemotherapy of Advanced Carcinoma of the Breast with Rubidazone (Phase II Study).

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 78/10

TECHNICAL OBJECTIVE

To determine the efficacy and toxicity of rubidazone as determined by response rate and median duration of response in patients with disseminated carcinoma of the breast who have not received prior therapy with adriamycin or other anthracycline antibiotics alone or in combination.

METHOD

Patient Eligibility: Patients with a life expectancy of six weeks with histologically proven advanced metastatic breast cancer who have not previously received adriamycin or other anthracycline antibiotics. Patients with symptomatic noncompensated congestive heart failure or primary myocardial disease are excluded because of possible cardiotoxicity. Patients must have been off radiotherapy or chemotherapy for four weeks prior to entering study. Prior surgical hormonal manipulation or medical hormonal therapy must have taken place six weeks before entering study. Patient must have increasing disease. Patients must have adequate bone marrow function, liver function, and renal function. Treatment with mithramycin is allowed. Adrenal steroids may be used for replacement purposes and temporarily in patients with hypercalcemia. No other chemotherapeutic agents may be given concomitantly.

Treatment 1: Good Risk

≤ 65 years of age; WBC ≥ 4000; platelets ≥150,000; no previous RT or marked tolerance to prior CT. Patients will be pretreated with benadryl 50 mg or phenergan 25 mg IV. Rubidazone 150 mg/M^2 IV q 3 weeks.

Treatment 2: Poor Risk

>65 years old; WBC 2500-4000; platelets 75,000-149,000; extensive RT or marked previous intolerance to CT.

SWOG 7726 - Stutz

Rubidazone: 25% reduction (112 mg/M^2) for bilirubin >2 <3, or if SGOT or SGPT is >3 times normal. 50% reduction for bilirubin >3. Creatinine >2 = 25% reduction. Other "poor risk" patients will start at a 25% dose reduction.

Dose modifications and adjustments as listed in the protocol.

PROGRESS

(78 02 - 78 09) One patient was on the study for six weeks (2 courses) with progressive disease while on treatment.

STATUS: (O)

TITLE: SWOG 7727/28, Combination Chemoimmunotherapy Utilizing BCNU, Hydroxyurea, and DTIC (BHD) with Levamisole versus DTIC Plus Actinomycin-D in the Treatment of Patients with Disseminated Malignant Melanoma, Phase III.

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 78/12

TECHNICAL OBJECTIVE

To determine remission induction rates, remission duration, survival, and toxicity in patients with disseminated malignant melanoma treated with BHD (BCNU, hydroxyurea, DTIC), BHD plus levamisole, and intermittent single high dose DTIC plus actinomycin D in a prospective, randomized clinical study.

METHOD

Patient Eligibility: histologically proven disseminated malignant melanoma with no previous treatment with any of the agents involved; measurable disease and estimated survival of at least two months; adequate renal and hepatic function; BUN >25 mg% or creatinine >1.5 mg% and bilirubin >2.5 mg%; hepatic or renal metastases are eligible provided organ function is adequate; recovery from the toxic effects of prior therapy and completion of RT to bone marrow bearing areas at least two weeks prior to entry.

Brain metastasis treatment: decadron 8-12 mg/day x 3 PO then tapered at the discretion of the investigator; day 3 begin total irradiation, 4000 rads over 2 week period; chemotherapy or chemoimmunotherapy will begin on the second week of radiotherapy.

Hepatic metastasis treatment: hepatic artery cannulation via femoral artery or brachial artery route. DTIC 200 mg/M^2/day over 24 hr infusion in 1000 ml of D_5W x 5 days; after 5-7 days patient will begin either chemotherapy or chemoimmunotherapy.

Patients will be stratified according to performance status and age. Treatment arms: I. (a) BHD - normal marrow (b) imparired marrow; II. (a) BHD + levamisole - normal marrow (b) impaired marrow; and III. (a) actinomycin D + high dose DTIC - normal marrow (b) imparied marrow.

If patients on BHD + levamisole or actinomycin D + DTIC have no response in the 2 initial courses, they will be crossed over. Patients not responding to BHD alone will be taken off study after an adequate trial. Dosages, courses of treatment, and

modifications are given in detail in the protocol.

PROGRESS

(78 02 - 78 09) One patient has been on the study one month. Therefore, it is too soon to draw any conclusions.

STATUS: (O)

TITLE: SWOG 7731, Anguidine in Adults with Advanced Soft Tissue and Bony Sarcomas

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 78/13

TECHNICAL OBJECTIVE

To determine the level of efficacy of the drug anguidine as a single agent in the treatment of advanced soft tissue and bony sarcomas in patients who have failed to respond or have relapsed on other therapeutic regimens.

METHOD

Patient Eligibility: diagnosis of soft tissue or bony sarcoma confirmed by pathologic examination of tissue; must demonstrate either primary or recurrent disease which is not amenable to control with surgery, radiotherapy, or higher priority chemotherapy; patients with prior surgery, radiation or chemotherapy are eligible if they have received no prior therapy with anguidine; patient must have measurable disease which can be followed for evidence of response; pretreatment WBC >3000/mcl; granulocytes >2000/mcl; platelets >100,000/mcl; normal hepatic function and normal renal function; patient must have been off prior chemotherapy or radiation long enough to recover from adverse effects (minimum 3 weeks); life expectancy of at least 6 weeks and performance status of at least 50% of the Karnofsky scale.

Treatment plan: all patients will recieve: anguidine 4.5 mg/M^2 IV over 4 hr daily for 5 days. These courses will be repeated every 3 weeks as long as disease does not progress and adverse effects permit continuation.

PROGRESS

(78 02 - 78 09) No patients have been entered on this study.

STATUS: (O)

TITLE: SWOG 7730, Cis-diamminedichloroplatinum in Refractory Disseminated Malignant Melanoma

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 78/14

TECHNICAL OBJECTIVE

To determine the efficacy of high intermittent doses of cis-diamminedichloroplatinum in patients with advanced malignant melanoma refractory to higher priority protocols and to determine the nature and extent of toxicity of this agent with the use of IV hydration only or IV hydration and mannitol diuresis.

METHOD

Patient Eligibility: Patients with histologically confirmed diagnosis of malignant melanoma who have not been treated with cis-diamminedichloroplatinum (CACP) before and who have an expected survival of 10 weeks are eligible for this study. Patients must have metastatic disease and measurable lesions refractory to higher priority protocols for malignant melanoma. Patients must have BUN $\leq$20 gm%, creatinine $\leq$1.7% with a creatinine clearance of at least 60 cc/min, absolute granulocyte count $\geq$2000/mm^3, platelet count $\geq$100,000/mm^3, and no evidence of obstructive uropathy as determined by IVP or renogram scan. Patients must have been off all previous chemotherapy for three weeks prior to entering the study, and the blood count nadirs must have been passed.

Treatment: Patients will be randomized to receive CACP + hydration or CACP + mannitol + hydration. Each group will receive allopurinol 300 mg PO/day started on admission to the hospital and continued as long as patient is on study; 2000 cc D_5 1/2NS given IV over 24 hours one day prior to CACP therapy; an initial dose of CACP 100 mg/M^2 IV over 10-15 minutes; and on the day of CACP therapy 2000 cc D_5 1/2NS IV plus additional IV fluids to match any emesis and continued over an additional 24 hour period following therapy. For those patients randomized on hydration only, 1000 cc of D_5W over 6 hours following CACP will be given in addition to other fluids. Patients randomized to

diuresis and hydration will be given a bolus injection of 12.5 gm mannitol just prior to CACP injection and followed by 25 gm mannitol in 1000 cc D_5W over 6 hours. Dose adjustments will be made as necessary. Therapy is to be repeated, until progression or relapse occurs, at 21 day intervals or delayed until there is adequate hematologic recovery.

PROGRESS

(78 02 - 78 09) No patients have been entered on this study.

STATUS: (O)

TITLE: SWOG 7707, Chemotherapy of Previously Treated Lymphoma Patients Using VBAP

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 78/15

TECHNICAL OBJECTIVE

To evaluate the frequency and completeness of response to VBAP chemotherapy (vincristine, BCNU, adriamycin, prednisone) in patients with malignant lymphoma (non-Hodgkin's disease and Hodgkin's disease) who have received prior therapy and are not eligible for higher priority studies.

METHOD

Patient Eligibility: Patients who have Hodgkin's disease or non-Hodgkin's lymphoma with measurable tumor and who have become refractory to prior treatment and are ineligible for higher priority. Patients should not have received prior myelosuppressive therapy for at least three weeks prior to this study. Prior nitrosourea or adriamycin therapy does not exclude patients so long as the cumulative dose of adriamycin does not exceed 390 mg/M^2. If prior therapy with vincristine resulted in permanent neurotoxicity, this agent will be deleted. Patients with history of myocardial disease are ineligible.

Treatment: These courses will be given in 21-day intervals if the blood counts are no lower than at onset of treatment:

VBAP	DAY: 1	2	3	4
Vincristine (total dose) IV	1 mg			
BCNU mg/M^2 IV	30			
Adriamycin mg/M^2	30			
Prednisone mg/M^2, PO	60	60	60	60

The program will be continued so long as there is stable or improving disease. Adequate trial is two courses. Should remission be achieved then the medications wil continue to maximum adriamycin tolerance (450 mg/M^2).

PROGRESS

(78 05 - 78 09) One patient on protocol for 5 months with partial response.

STATUS: (O)

TITLE: SWOG 7725, Continuous 5-Drug Induction with Intermittent CMPF vs CMPF + Levamisole for Maintenance in Patients with Estrogen Receptor Negative Breast Cancer, Phase III.

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 78/16

TECHNICAL OBJECTIVE

To determine the respective effects of levamisole on the duration of response and survival of patients with advanced breast cancer concurrently treated with maintenance chemotherapy after a successful remission induction trial of continuous Cooper regimen; and to accumulate data on immunologic variables under the conditions of chemotherapy alone and combined chemotherapy and immunotherapy with levamisole of advanced breast cancer.

METHOD

Patient Eligibility: only patients proven to be estrogen receptor negative are eligible. Patients must have a life expectancy of 2 months and measurable lesions and no previous chemotherapy other than adjuvant chemotherapy. Patients coming off additive hormonal therapy and antiestrogens must have been off therapy for 6 weeks and have increasing disease. If the 6 week observation period off hormones appears to be excessively risky, the patient may be entered provided that 3 weeks have elapsed since last day of hormonal therapy and disease is rapidly progressive. Prior surgical ablative endocrine therapy must have taken place 3 weeks prior to entry if the disease is rapidly progressive and 10 weeks if slowly progressive. Patients with previous cancer immunotherapy or who had relapsed while receiving multiple durg adjuvant chemotherapy are ineligible. Concomitant therapy with mithramycin is not allowed, and concomitant therapy with corticosteroids (other than prednisone) is allowed only in adrenalectomized or hypophysectomized patients.

Treatment: All patients will undergo a remission induction trial with continuous Cooper regimen in the following fashion:

Vincristine	0.625 mg/M^2	IV once a week for 8 weeks
5-Fluorouracil	300 mg/M^2	IV " " " "
Methotrexate	15 mg/M^2	IV " " " "
Cyclophosphamide	60 mg/M^2	PO daily for 8 weeks
Prednisone	30 mg/M^2	PO daily for 2 weeks, reduce to
	20 mg/M^2	PO for next 2 weeks, reduce to
	10 mg/M^2	until day 49, then taper to nothing by day 56

Patients with increasing disease after 6 weekly induction cycles will go off study. After achievement of remission or stable status, the patients will be randomly allocated to the following treatment arms:

Arm I - Maintenance "Intermittent Cooper Regimen"

5-Fluorouracil	180 mg/M^2	PO daily x 5 days, q 28 days
Methotrexate	4 mg/M^2	PO " " " "
Cyclophosphamide	120 mg/M^2	PO " " " "
Prednisone	40 mg/M^2	PO " " " "

Arm II - Intermittent Cooper + levamisole

The same as Arm 1 plus levamisole 100 mg/M^2 daily in 3 divided doses on days 4-6, 11-13, and 18-20 of each cycle.

As with all studies, dose modifications will be made when necessary.

PROGRESS

(78 02 - 78 09) One patient was treated for eight weeks with disease progression. One patient has been on the study for one month which does not allow enough time to study for results.

STATUS: (O)

TITLE: SWOG 7717, Management of Patients with a Metastatic Adenocarcinoma of Unknown Origin, Phase II

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 78/17

TECHNICAL OBJECTIVE

To determine the yeild of various diagnostic procedures in finding the site of tumor origin in patients who present with metastatic adenocarcinoma with no obvious primary source; to compare the efficacy of combination chemotherapy using fluorouracil, adriamycin, and cytoxan vs fluorouracil alone in the palliative management of patients with metastatic adenocarcinoma of unknown origin; and to assess the hematologic toxicity of the chemotherapy regimen on treated patients.

METHOD

Patient Eligibility: histopathologic confirmation of metastatic adenocarcinoma with no obvious primary source. Patients must have measurable disease and expected sruvival of 6 weeks and have had no prior chemotherapy. The WBC must be >4000/µl and platelet count >100,000/µl.

After diagnostic studies as outlined in the protocol (para 5) to establish tumor site, the patients will be randomized to one of the following treatment schedules:

Schedule I: adriamycin, 40 mg/M^2, IV on day 1, q 28 days
5-FU, 1000 mg/M^2/day x 4 as continuous IV infusion, q 28 days
cytoxan, 400 mg/M^2, IV on day 1, q 28 days

If patient achieves a partial regression of measurable tumor, 5-FU administration may be changed to: 500 mg/M^2, IV weekly.

Schedule II; 5-FU, 1000 mg/M^2/day x 4 continuous IV, q 28 days.

If the patient achieves a partial regression of measurable tumor, 5-FU administration may be changed to 500 mg/M^2, IV weekly at the discretion of the investigator.

PROGRESS

(78 02 - 78 09) One patient treated for 2 courses with progression of disease while on treatment.

STATUS: (O)

TITLE: SWOG 7724, Diglycoaldehyde in Metastatic Malignant Melanoma

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 78/18

TECHNICAL OBJECTIVE

To evaluate the response of metastatic malignant melanoma to diglycoaldehyde and to study the toxicity of the drugs.

METHOD

Patient Eligibility: patients with disseminated disease who have relapsed or are resistant to regimens in a higher priority. Patients must have a serum creatinine $\leq$1.5 mg%, BUN $\leq$20 mg%, platelet count $\geq$150,000/mm^3, and WBC $\geq$4,000/mm^3.

Treatment: Diglycoaldehyde will be administered in daily doses of 1.5 gm/M^2 as a six hour intravenous infusion in 5% dextrose in water for five days. Courses will be repeated at three week intervals when possible. Second and third courses of the drug will only be administered when the WBC is $\geq$4000 and the platelet count is $\geq$150,000. No course will be commenced until any proteinuria has disappeared and until the BUN has fallen to a measurement $\leq$20 and the creatinine is $\leq$1.5. An adequate trial consists of two courses of therapy. Patients who exhibit progressive disease after two courses or who relapse from remission after two courses will be removed from the study. Patients whose BUN and creatinine remain greater than 20 and greater than 1.5, respectively, or who exhibit greater trace proteinuria for greater than five weeks post therapy will be removed from the study.

PROGRESS

(78 02 - 78 09) No patients have been entered on this study.

STATUS: (O)

TITLE: SWOG 7716, Tamoxifen in Renal Cell Carcinoma

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO. 78/28

TECHNICAL OBJECTIVE

To determine the response rate and survival in patients with disseminated renal cell carcinoma treated with tamoxifen.

METHOD

Patient Eligibility: patients with histologically proven disseminated renal cell carcinoma who have received no antiestrogen agents and who have an expected survival of 8 weeks. Patients with measurable disease no longer amenable to surgery or radiotherapy who have been off all previous chemotherapy or hormonal therapy for four weeks with clearly progressive disease. Radiotherapy to the pilot lesion must have been completed 3 weeks prior to entry. Bone lesions which have received radiotherapy at anytime are ineligible.

Treatment: Tamoxifen will be given 10 mg BID orally for at least 6 weeks. If objective remission is obtained, treatment is continued until disease progression is obvious. If the lesions are static, therapy is to be continued, but reevaluation at 6-week intervals until objective remission or progression is obtained. In case of definite tumor progression after adequate therapy or severe or unusual side effects, therapy will be stopped.

PROGRESS

(78 03 - 78 09) One patient on protocol for 2+ months with progressive disease while on treatment.

STATUS: (O)

TITLE: SWOG 7732, The Effect of CMF With and Without Tamoxifen in Patients with Estrogen Receptor Positive Breast Cancer, Phase III.

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 78/29

TECHNICAL OBJECTIVE

To determine if the antiestrogen, tamoxifen, in combination with Cytoxan, methotrexate, and 5-FU will alter the response rate, duration of response, and median survival seen with Cytoxan, methotrexate, and 5-FU alone in advanced human breast cancer in patients who are estrogen receptor positive.

METHOD

Patient Eligibility: histological proof of progressing recurrent breast cancer, measurable disease, and estimated survival greater than 10 weeks. On assay of primary or recurrent tumor, estrogen receptor must be present. WBC must be $\geq$4000, platelet $\geq$100,000, hematocrit $\geq$30; patients having abnormal creatinine and BUN >30 or creatinine clearance <60 are ineligible. Patients with abnormal liver function tests must have liver scan or biopsy to diagnose liver metastasis if not previously established. Prior hormonal therapy will be allowed if it was completed 4 weeks prior to entry and there is evidence of clearly progressive disease. Glucocorticoids will be allowed as replacement therapy only after adrenalectomy. Patients with prior Cytoxan, methotrexate, or 5-FU therapy; endocrine ablation less than 4 weeks prior to entry; or radiotherapy to measurable lesion within 6 weeks of entry are ineligible. Previously radiated bone lesions may not be used as the pilot lesion.

Treatment: Patients will be randomized between CMF + tamoxifen and CMF alone as shown below:

Arm I - CMF + Tamoxifen

Tamoxifen, 10mg, BID PO daily; Cytoxan 65 mg/M^2 PO daily; methotrexate 15 mg/M^2 IV weekly; 5-FU 300 mg/M^2 IV weekly.

Arm II - CMF alone - the same treatment plan as Arm I without Tamoxifen.

SWOG 7732 - Stutz

Dose adjustments will be based on nadir counts.

PROGRESS

(78 03 - 78 09) No patients have been entered on this study.

STATUS: (O)

TITLE: SWOG 7735, Anguidine in Advanced Gastrointestinal Malignancies

PRINCIPAL INVESTIGATOR: LTC Firedrich H. Stutz, MC

WORK UNIT NO: 78/30

TECHNICAL OBJECTIVE

To determine the efficacy of anguidine and survival in terms of response rate and median duration of response in the treatment of advanced gastrointestinal malignancies; and to observe any factors predisposing to excessive myelosuppression and for other toxicities not observed during Phase I studies of this drug.

METHOD

Patient eligibility: all patients with histologically proven gastrointestinal malignancies coming off of or not eligible for higher priority studies. Patients with life expectancy of greater than 6 weeks who have surgically incurable disease and objectively measurable parameters. Patients should not have received extensive radiation or chemotherapy within the preceding 21 days (42 days with nitrosourea). If patient has had recent surgery involving resection of gastrointestinal tract, entry should wait at least 3 weeks or until return of bowel function. Serum creatinine should be <2.0 mg%, BUN <30 mg%, and serum bilirubin <6.0 mg%. Patients with active wound infections are ineligible.

Treatment: Patients will be divided into poor risk and good risk categories; poor risk - >65 years, poor tolerance to prior chemotherapy, extensive prior radiation, serum bilirubin between 3.0 and 6.0 mg% or hepatic enzyme elevation of greater than three times the institutional normal; good risk - all other patients.

Good Risk Patients: 4.5 mg/M^2 (dissolved with 500 ml of D_5W) IV daily for 5 days.

Poor Risk Patients: 3.0 mg/M^2 (dissolved with 500 ml of D_5W) IV daily for 5 days.

Body surface area calculations will be based on ideal body weight in cases of massive obesity or ascites. Subsequent courses of treatment will be administered at intervals of 28 days as tolerated and should not be repeated until the nadir of the granulocyte and/or platelet count has recovered to at least 2,000/mm^3 and 100,000/mm^3, respectively. If after 3 days of treatment in any cycle, the WBC drops below 4,000 (granulocytes <2,000) or platelets drop below 100,000, the remaining treatment for that cycle shall not be given. Blood pressure determinations will be obtained prior to and immediately following each daily infusion. An adequate trial will consist of two courses of treatment. In the presence of tumor response or disease stabilization, courses will be repeated at 4-week intervals with any necessary dose adjustments.

PROGRESS

(78 03 - 78 09) One patient on study for six weeks; too early for response evaluation.

STATUS: (O)

TITLE: SWOG 7736, Evaluation of Anguidine in the Treatment of Urological Malignancies, Phase II.

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 78/31

TECHNICAL OBJECTIVE

To determine the efficacy of anguidine in treating the major urological malignancies in terms of response rate, duration or response, and survival; to more fully study the adverse effects of anguidine and factors important in producing such effects.

METHOD

Patient Eligibility: patients with histologically proven advanced urological malignancies not eligible for treatment with drugs of proven or likely higher efficacy with a life expectancy of at least 6 weeks. Measurable lesions are mandatory. WBC >4,000/mm^3, platelet count >100,000/mm^3, serum bilirubin <6.0, BUN <40 mg/ml, and serum creatinine <2.0 mg/dl. No radiotherapy or chemotherapy during preceding 21 days (42 days if nitrosourea) and recovered from acute toxicities of such treatment. Previous hormonal therapy in renal cell cancer is allowed, but should be stopped before entry.

Treatment: Patients will be divided into poor risk and good risk categories as defined in protocol. Anguidine must be dissolved with 500 ml of D_5W and administered as an IV infusion over a period of 4 hours. The initial dose level will be as follows: Good risk: 4.5 mg/M^2 x 5 days
Poor Risk: 3.0 mg/M^2 x 5 days
Subsequent courses of treatment will be administered for 5 days at intervals of 28 days as tolerated, if the nadirs have been passed and the granulocyte count is >2000 and platelets >100,000. Dose modification will be made as required. An adequate trial of therapy will consist of one cycle of chemotherapy with evidence of increasing disease in the face of toxicity. Patients with improving disease or stable disease will continue treatment indefinitely with the proper dose adjustment.

SWOG 7736 - Stutz

PROGRESS

(78 03 - 78 09) No patients entered on this study.

STATUS: (O)

TITLE: SWOG 7738, Combination Chemotherapy of Pancreatic Adenocarcinoma with Mitomycin-C, 5-FU, and Streptozotocin, Phase III.

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 78/32

TECHNICAL OBJECTIVE

To determine and document the response rates and toxicity of mitomycin-C, streptozotocin, and 5-fluorouracil in the management of disseminated pancreatic adenocarcinoma.

METHOD

Patient Eligibility: patients with histologically confirmed adenocarcinoma of the exocrine pancreas and with distant metastases and/or extension of the disease is outside of a port size >15 x 15 cm. Patients with prior exposure to mitomycin-C or streptozotocin are ineligible. Adequate renal function as evidenced by a BUN <25 mg% and a creatinine of <2.0 mg%. Patients with diabetes are eligible.

Treatment 1: Good risk - 5-FU, 1000mg/M^2 given as a continuous 24 hour infusion on days 1-4 and 29-32; mito-C, 15.0 mg/M^2 by IV bolus through a well established IV on day 1.

Treatment 2: Good Risk - 5-FU, as in Treatment 1; mito-C as in Treatment 1; streptozotocin, 400 mg/M^2 by IV bolus on days 1-4 and 29-32.

Treatment 3: Poor Risk - Same as Treatment 1 except mito-C starting dose will be 10.0 mg/M^2.

Treatment 4: Poor Risk - Same as Treatment 2 except mito-C starting dose will be 10.0 mg/M^2.

Dose adjustments will be made as required. A single cycle of therapy will be considered an adequate trial. Patients whose disease has remained stable or in whom a response has occurred will be continued on this regimen until progressive disease is documented.

PROGRESS

(78 06 - 78 09) No patients entered on this study.

STATUS: (O)

TITLE: SWOG 7806, Cis-Diamminodichloroplatinum (II) in the Treatment of Refractory Epidermoid Carcinoma of the Esophagus, Phase II.

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 78/35

TECHNICAL OBJECTIVE

To determine the response rate and survival, with some degree of precision, utilizing cis-diamminodichloroplatinum II (CACP) in the treatment of patients with squamous cell carcinoma of the esophagus which is growing despite more standard therapy.

METHOD

Patient Eligibility: Patient must have biopsy confirmed diagnosis of epidermoid carcinoma of the esophagus. Adenocarcinoma of the esophagus is not eligible. Patient must have an absolute granulocyte count of $\geq$2,000 and a platelet count of $\geq$150,000 and must be past the present nadir resulting from any prior therapy. Patient must have a BUN of no higher than 20 mg% and a serum creatinine no higher than 1.4 mg% or creatinine clearance in excess of 75 cc/minute. Two functioning kidneys and an unobstructed urinary tract are required.

Treatment: CACP 50 mg/M^2 IV infusion over an 1-4 hour interval, days 1 & 8 of each 28 day course. Prior to every dose, the patient must receive at least 1,000 cc of fluids above usual intake (also on the evening before administration).

As long as there is evidence of tumor regression or disease stability at an acceptable level without unacceptable toxicity the CACP will be continued indefinitely. Although 30 days on therapy will constitute an adequate tiral, an attempt will be made to give each patient two complete courses if the clinical status is acceptable.

PROGRESS

(78 09 - 78 09) No patients entered on the study.

STATUS: (O)

TITLE: SWOG 7807, CACP in Refractory Epidermoid Carcinoma of the Lung

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 78/36

TECHNICAL OBJECTIVE

To determine the response rate and survival in patients with epidermoid carcinoma of the lung who have demonstrated refractoriness to previous therapy, utilizing cis-diammino-dichloroplatinum (II) (CACP).

METHOD

Patient Eligibility: Patients must have confirmed, preferably by biopsy, epidermoid carcinoma of the lung; an absolute granulocyte count of at least 2,000, a platelet count of at least 150,000, and must be past the nadir resulting from any prior therapy; a BUN >20 mg%, serum creatinine >1.4 mg% (if these two criteria are not met, a patient will be considered eligible if the creatinine clearance proves to be in excess of 75 cc/min); no evidence of obstruction of the urinary tract as determined by radiographic studies; and measurable disease.

Treatment: On the evening before and prior to drug administration, the patient will receive at least 1000 cc of fluids above usual intake (either IV or oral). The initial course will be given at a dose of 50 mg/M^2 IV infusion with the drug diluted in 1 liter D5½NS. This will be given on days 1 & 8, over an interval of 1-4 hours. The course will be repeated at four week intervals if BUN and serum creatinine and blood counts are at defined levels. For subsequent courses the drug dose will be modified based on the effects of the immediate previous course. CACP therapy will be continued indefinitely as long as there is evidence of tumor regression or disease stability at an acceptable level. Although 30 days on study will constitute an adequate trial, an attempt will be made, if clinically tenable, to maintain a patient on study for two complete courses.

PROGRESS

(78 09 - 78 09) One patient entered on study, but has not been on study long enough for evaluation of results.

STATUS: (O)

TITLE: SWOG 7804, Adjuvant Chemotherapy with 5-Fluorouracil, Adriamycin, and Mitomycin-C (FAM) vs Surgery Alone for Patients with Locally Advanced Gastric Adenocarcinoma

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 78/42

TECHNICAL OBJECTIVE

To determine the efficacy of adjuvant chemotherapy with FAM on the disease-free interval and survival of patients with TNM stage-groups IB, IC, II and III gastric adenocarcinoma compared to potentially curative surgery alone.

METHOD

Patient Eligibility: patients must have TNM stage-group IB, IC, II or III gastric adenocarcinoma and no microscopic or gross residual postoperatively; no prior chemo- or radiotherapy; no medical contraindications to chemotherapy with FAM; serum bilirubin <2.0 mg/100 ml; SGOT and SGPT less than three times the upper limit of normal values; creatinine clearance >75 cc/min; BUN ≤25 mg%; serum creatinine ≤1.5 mg%; WBC >4,000; and platelets >100,000.

Treatment: After surgery, patients will be randomized to either Treatment 1 (no further therapy) of Treatment 2:
FAM - 5-FU, 600 mg/M^2 IV days 1 & 8, 29 & 36
adriamycin, 30 mg/M^2 IV days 1 & 29
mitomycin-C, 10 mg/M^2 IV day 1

A total of 6 courses, one every 8 weeks, will be administered. After 12 months, the active therapy phase is completed. The patient will be followed at six month intervals for five years if remission continues.

PROGRESS

(78 07 - 78 09) No patients entered on this study.

STATUS: (O)

TITLE: SWOG 7809, Maytansine (NSC-153858) Therapy of Advanced Breast Cancer, Phase II.

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 78/43

TECHNICAL OBJECTIVE

To evaluate the effectiveness of maytansine in terms of response rate and survival in patients with breast cancer resistant to standard therapeutic modalities.

METHOD

Patient Eligibility: Patients with histologically proven breast cancer resistant to known effective agents; expected survival of 6 weeks; either disease progression on prior therapy or have received no hormonal or chemotherapy or radiation therapy to the measurable lesion for at least 4 weeks; and measurable disease. Patients having received prior vincristine therapy will be analyzed separately.

Treatment I: Good Risk Patients: 0.5 mg/M^2/day x 5 days IV every 21 days

Treatment II: Poor Risk Patients: 0.3 mg/M^2/day x 5 days IV every 21 days

Poor risk defined as patients with liver metastasis or abnormal liver function.

Drug dosage will be increased every other treatment as outlined in para 5.0 of the protocol.

Duration of treatment: (1) terminated if increasing disease after two courses of therapy; (2) terminated if severe or life-threatening toxicity; (3) terminated upon relapse; (4) terminated if stable disease after three courses of therapy at physician's discretion.

PROGRESS

(78 08 - 78 09) No patients entered on study.

STATUS: (O)

TITLE: SWOG 7814, A Comparison of Methotrexate and Cis-Platinum for Patients with Advanced Squamous Cell Carcinoma of the Head and Neck Region

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 78/46

TECHNICAL OBJECTIVE

To determine whether cis-platinum will give a superior response rate and/or a longer remission duration than methotrexate in patients with squamous cell carcinoma of the head and neck region. SWOG 7814 combines the two best treatments of previously approved SWOG protocols, 7519 and 7629, which it replaces.

METHOD

Patient Eligibility: patients with histologically proven advanced squamous cell carcinoma of the head and neck region which is not amenable to other forms of therapy and with measurable tumor lesions; no prior methotrexate or cis-platinum therapy; objective evidence of disease progression 3 weeks or more after discontinuation of any prior radiotherapy or chemotherapy; life expectancy of 8 weeks or more; creatinine clearance of $\geq$50 cc/1.73 M^2/min; WBC of $\geq$4,000, platelets >125,000, and optional bone marrow biopsy to assess adequacy of bone marrow reserve.

Patients will be randomized to receive either:

Treatment 1: methotrexate alone, 15 mg/M^2 IM daly x 3 days, every 3 weeks
Treatment 2: cis-platinum alone, 50 mg/M^2, days 1 & 8, every 4 weeks

Adequate treatment: patients must receive two complete cycles of therapy showing some biological activity from the drug. Patients will be removed from study if: increasing disease following the initial treatment cycle or the second cycle as manifested by at least Grade 2 toxicity. Patients with no change in their measurable disease may be continued on study at the discretion of the investigator. Patients will be removed from study following progression of disease.

PROGRESS

(78 09 - 78 09) No patients entered on study.

STATUS: (O)

TITLE: SWOG 7808, Combination Modality Treatment for Stages III and IV Hodgkin's Disease, MOPP #6

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 78/47

TECHNICAL OBJECTIVE

To attempt to increase the complete remission rate induced with MOP-BAP (nitrogen mustard, vincristine, procarbazine, prednisone, adriamycin, and bleomycin) alone utilizing involved field radiotherapy in patients with Stages III and IV Hodgkin's disease achieving partial remission at the end of 6 cycles.

To determine if immunotherapy maintenance with levamisole or consolidation with low dose involved field radiotherapy will produce significantly longer remission durations over a no further treatment group when complete remission has been induced with 6 cycles of MOP-BAP in Stages III & IV Hodgkin's.

METHOD

Patient Eligibility: Patients must have histologic diagnosis of Hodgkin's disease classified by the Lukes and Butler System; no prior chemotherapy; 15 years of age or older. Patients with a history of congestive heart failure, valvular heart disease, or serious obstructive or restrictive pulmonay disease will be excluded.

Treatment: All patients except those with prior radiotherapy must receive radiation therapy consultation before chemotherapy is started.

Treatment 1: Normal marrow patients will receive 6 cycles of MOP-BAP

Treatment 2: Imparied bone marrow patients will receive 6 cycles of MOP-BAP with dose modifications.

Complete remission (CR) patients will be randomized between Treatment 3 (no treatment) and Treatment 4 (levamisole). Partial remission (PR) patients without prior radiation therapy or residual bone marrow involvement will receive Treatment 6 (radiation therapy). PR patients with prior radiation therapy or those with residual bone marrow involvement will receive treatment 7 (4 additional cycles of MOP-BAP; after 10 total cycles of MOP-BAP, patient will continue study on MOP-BAP therapy at the discretion of the investigator). CR patients without prior radiation therapy will receive Treatment 5 (radiation therapy for CR). Doses for chemotherapy and radiotherapy can be found in para 5.0 of the protocol.

SWOG 7808 - Stutz

PROGRESS

(78 09 - 78 09) No patients entered on study.

STATUS: (O)

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